The Economic Burden of Diabetes in Ireland

A thesis submitted to the National University of Ireland, Cork for the degree of Doctor of Philosophy in the School of Public Health.

Coláiste na hOllscoile Corcaigh,
University College Cork, Ireland

October 2018

Kate Nuala O'Neill

BSc (Public Health & Health Promotion), MPhil (Epidemiology)

Head of School

Professor Ivan J. Perry

Supervisors

Professor Patricia M. Kearney
Dr Sheena M. McHugh
Dr Anthony P. Fitzgerald

Table of Contents

List of Tables

List of Figures

List of Abbreviations

AIC - Akaike Information Criterion

AME – Average Marginal Effect

BIC - Bayesian Information Criterion

BMI – Body Mass Index

CAPI - Computer Assisted Personal Interview

CI – Confidence Interval

CSO – Central Statistics Office

DPS – Drugs Payment Scheme

FFQ – Food Frequency Questionnaire

GDP – Gross Domestic Product

GMS – General Medical Scheme

GP – General Practitioner

HSE-PCRS – Health Service Executive – Primary Care Reimbursement Scheme

IRR – Incidence Rate Ratio

LTI – Long-Term Illness

OR – Odds Ratio

PIF – Potential Impact Fraction

PCOS - Polycystic Ovarian Syndrome

SD – Standard Deviation

SLAN – Survey of Lifestyle, Attitudes and Nutrition

SSB – Sugar-Sweetened Beverages

TILDA – The Irish LongituDinal study of Ageing

UI – Uncertainty Interval

VAT –Value Added Tax

WHO-ATC - World Health Organisation - Anatomic Therapeutic Classification codes

Declaration

I declare that this thesis has not been submitted for another degree, either at University College Cork or elsewhere. All external references and sources are clearly acknowledged and identified within the contents. I have read and understood the regulations of University College Cork concerning plagiarism.

Signed: **Date:**

Acknowledgements

I would like to express my gratitude to my three supervisors, Professor Patricia Kearney, Dr Sheena McHugh and Dr Tony Fitzgerald. I have thoroughly enjoyed my time at UCC and my positive experience is testament to your unwavering support and guidance throughout the last three years. I have gained invaluable knowledge and experience under your supervision and I look forward to working together in the future.

To all at The School of Public Health who have been terrific colleagues and friends over the past few years, and who contribute to such an open, supportive and motivating work environment. A special word of thanks to Marsha, Caroline, Fiona and Emmy for your friendship and to Ber, who is a constant source of encouragement and always on hand to solve any issue!

I would like to thank my close friends and family for their understanding and patience when I bored them with the details of my PhD! They were always there at the drop of a hat to provide me with a much needed break – it didn't take much convincing!

To my parents, Ellen and Sam. You have both been such an inspiration to me and your constant encouragement and support has led me to where I am today. Mom, I will never be able to express in words my gratitude for all you have done and continue to do for us. I would not be here today if you had not spotted the BSc in Public Health on the CAO list many years ago! Dad, I would be lost without you – any problem that ever arises you are there to sort it out! Your constant presence and support over the last few months has enabled me to concentrate on getting the PhD finished – nothing is too much an ask.

Jonathan – where do I start! Right from the beginning of this journey from my masters at Cambridge to surviving on a PhD stipend, you have been nothing but supportive. I could not have achieved this without you and I will be forever grateful.

Thesis Abstract

Background and Aims

As a leading cause of morbidity and mortality, diabetes places a significant burden on society and presents a growing challenge for national economies. The economic burden of diabetes is forecast to grow in coming years, driven by increasing diabetes prevalence and rising medical expenditure. Worldwide, there is a lack of robust, comprehensive and comparable estimates of costs attributable to diabetes. Cost-effective interventions are required to efficiently manage and treat diabetes and curb increasing trends in incidence. Three effective interventions spanning the prevention continuum have recently been recommended in Irish health policy and can potentially influence the burden of diabetes; a sugar-sweetened beverage (SSB) levy, financial remuneration for the provision of structured diabetes care in primary care through the 'cycle of care' initiative and bariatric surgery. The overarching aims of this thesis were to estimate the economic burden of diabetes in Ireland and to explore the potential for current policy approaches to impact on the burden of diabetes.

Methods

The economic burden of diabetes was estimated from a societal perspective employing an incremental costing approach where possible. Nationally representative data from The Irish LongituDinal study of Ageing (TILDA) and the national pharmacy claims database, Health Service Executive – Primary Care Reimbursement Service (PCRS), were utilised. Direct costs included health service utilisation costs and medication costs while indirect costs included productivity losses from reduced labour force participation and premature mortality. The impact of diabetes on health service utilisation and productivity were explored using multivariable regression models. Trends in pharmaceutical expenditure on diabetes between 2011 and 2015 were explored. Total expenditure associated with diabetes was calculated by extracting data on all diabetes-related items dispensed. A comparative risk assessment was

conducted to robustly estimate the potential impact of a reduction in population-level SSB consumption on type 2 diabetes incidence. Using data from the Survey of Lifestyle, Attitudes and Nutrition (SLAN), the potential impact of a 10% levy on SSBs was explored. An assessment of the potential impact of the ‘cycle of care’ and bariatric surgery provision on the burden of diabetes was conducted using a cross-sectional analysis of TILDA.

Results

Diabetes was associated with excess health service use across the entire health system and was also adversely associated with productivity. Compared to those without diabetes, people with diabetes have on average 1.49 (95% CI: 1.10, 1.88) additional GP visits annually. Diabetes was associated with an 87% increase in out-patient visits, 52% increase in hospital admissions and 33% increase in A&E attendances ($p<0.001$). People with diabetes were 41% less likely to be employed than those without diabetes ($p<0.001$). The total costs of diabetes in those aged over 50 years in Ireland was estimated at €545,787,911 (95% CI: 365,597,451 – 766,782,103) in 2013; €238,155,072 (95% CI: 192,023,954 – 278,959,992) in direct costs and €307,632,839 (95% CI: 173,573,497 – 487,822,111) in indirect costs. Over the five-year period from 2011 to 2015, the cost of prescription items used specifically in the treatment and management of diabetes increased by 18%, reaching €153,621,477 in 2015, with blood glucose-lowering medications accounting for 73% of this increase. The introduction of a 10% SSB levy is estimated to prevent 0.25% (95% UI: 0.01%,0.5%) of incident type 2 diabetes cases in a ten-year period. While the majority of people with type 2 diabetes are covered by the ‘cycle of care’ initiative, 31.6% (95% CI: 27.8, 35.6) are not eligible. Current eligibility criteria do not identity people on the basis of clinical need but rather on income. With fewer than 50 publicly funded bariatric surgeries taking place annually, current service provision meets less than 0.1% of the need.

Conclusion

Diabetes places a substantial burden on the Irish health system as well as the national economy. The estimates provide useful information to inform policy-level responses to tackle the burden of diabetes. With findings demonstrating increasing pharmaceutical expenditure on diabetes in recent years, combined with the increasing prevalence of diabetes in Ireland, the economic burden of diabetes is likely to increase. Population-level interventions targeting SSB consumption can play a role in the primary prevention of type 2 diabetes. The potential impact of effective tertiary prevention interventions, as recommended and supported by Irish health policy, are limited by inequitable and inadequate investment.

1. Introduction

1.1 Introduction

Diabetes is one of the most concerning global public health challenges of the 21st century (1). As a leading cause of morbidity and premature mortality, diabetes places a significant burden on society (2,3). The number of people with diabetes continues to increase, driven by population growth and ageing. Between 1980 and 2014, the number of adults with diabetes worldwide increased four-fold (4). The global economic burden of diabetes was estimated at $1.31 trillion (95% CI: 1.28, 1.36) in 2015, accounting for 1.8% of global Gross Domestic Product (GDP) (5). With increasing diabetes prevalence and rising medical expenditure, the costs of diabetes are forecast to continue to grow in coming years (6,7). Should current trends in diabetes prevalence and mortality continue, it is estimated that by 2030, the global burden will increase to $2.5 trillion (95% CI: 2.4, 2.6) (7). Medication costs have been identified as the primary driver of increasing medical expenditure on diabetes (8,9). While empirical evidence is scarce, it is suggested that the observed increase in pharmaceutical expenditure can be attributed to a combination of increasing diabetes prevalence, advancements in clinical guidelines advocating long-term glycaemic control and the upsurge of new expensive medical treatments (8–10).

Cost-of-illness studies provide important estimates highlighting the economic burden of diabetes. Such estimates motivate and inform the implementation of cost-effective strategies addressing the burden of diabetes. Worldwide, there is a lack of accurate, comprehensive and comparable estimates of costs attributable to diabetes (11). Valid and reliable incremental cost estimates for diabetes are required at a regional and country level to improve the accuracy of global cost of diabetes estimates (10).

Diabetes not only places a substantial burden on the health system but is also a concern for national economies (5). It highlights the urgent need for cost-effective interventions to efficiently manage diabetes and its complications (12). In tandem with this, the prevention of diabetes is essential to curb the increasing prevalence, ensuring that the future costs of diabetes are curtailed and improvements in rates of morbidity and mortality are realised in economic terms. A public health response to diabetes identifies three areas of prevention required to adequately address the burden of diabetes (10,13–18). Primary prevention employs a population-wide approach with the aim of intervening before the onset of diabetes occurs. Secondary prevention targets those at high risk of developing diabetes, while tertiary prevention strategies manage and treat diabetes once it has manifested with the aim to prevent diabetes-related complications. Effective interventions for diabetes exist across this continuum of prevention.

Three effective interventions spanning the prevention continuum have recently been addressed in Irish health policy and can potentially influence the burden of diabetes in Ireland. The primary prevention of diabetes has been addressed in healthy government policy tackling SSB consumption (19–21). Two effective tertiary prevention interventions have also been recommended; the provision of structured care for people with type 2 diabetes in primary care supported through an initiative called the "cycle of care" and the provision of bariatric surgery (22,23).

Valid estimates of the potential impact of public health interventions are essential to allow policy-makers make informed decisions about the cost-benefit trade-off between them (24). Furthermore, where robust evidence on effective interventions exist, the translation of this evidence into policy and the subsequent implementation into practice is essential (25). The impact of interventions is influenced by policy decisions including legislative change, for example, sugar-sweetened beverage (SSB) tax and health system changes such as, drug reimbursement decisions or financial remuneration for chronic disease management. Although research has provided evidence for preventing or delaying type 2 diabetes, health policy decisions influence their potential impact on the burden of diabetes (26).

1.2 Aims

The two main aims of this thesis were to estimate the economic burden of diabetes in Ireland and to explore the potential for health policy approaches to impact on the burden of diabetes.

1.3 Objectives

These aims were addressed by the six specific objectives outlined below;

1. to provide robust estimates of health service use and direct healthcare costs attributable to diabetes in Ireland.
2. to estimate the total costs, direct and indirect, attributable to diabetes in Ireland.
3. to explore trends in pharmaceutical expenditure on diabetes between 2011 and 2015, examining the impact of newer blood glucose-lowering medications.
4. to provide a robust estimate of the impact of sugar-sweetened beverage consumption on type 2 diabetes incidence and subsequently estimate the potential impact of public health interventions targeting sugar-sweetened beverage consumption.
5. to investigate the coverage of the cycle of care initiative and to describe the population who are not currently eligible.
6. to estimate the number of people who would potentially benefit from bariatric surgery in Ireland based on established clinical criteria.

1.4 Thesis outline

This thesis contains nine chapters, six of which are studies addressing the aims and objectives outlined above. Figure 1 illustrates the six studies and the corresponding chapters.

The global burden of diabetes and its implications are presented in Chapter 2. Trends in the epidemiology of diabetes are explored, specifically describing trends in prevalence, incidence and diabetes-related morbidity and mortality. The economic burden of diabetes is subsequently outlined with a discussion on the variation in methodologies used to estimate the cost of diabetes. Finally, the implications of the burden of diabetes are considered, identifying key approaches required to address the burden.

The excess health service use and related costs attributable to diabetes are described in Chapter 3. This study demonstrates the use of robust methods to provide the first estimates of excess health service utilisation attributable to diabetes in Ireland. The results are used in Chapter 4 to estimate the total economic burden of diabetes in Ireland. This study uses best available data and methods to estimate the direct and indirect costs attributable to diabetes in Ireland.

Chapter 5 examines trends in pharmaceutical expenditure on diabetes-related items between 2011 and 2015. This study uses data from a national pharmacy claims database and highlights the impact of newer blood glucose-lowering medications on expenditure. The impact of cost-containment measures implemented over the study period are also assessed.

The impact of a primary prevention strategy is explored in Chapter 6. This study provides robust estimates of the potential impact population-level interventions targeting sugar-sweetened beverage consumption can have on type 2 diabetes incidence in Ireland. Specifically, this study assesses the potential impact of the recently introduced sugar-sweetened beverage levy in curbing type 2 diabetes incidence.

Cost-effective interventions are also required to efficiently manage diabetes and related complications (10). The potential for two tertiary prevention strategies, as provided for in Irish health policy, to influence the burden of diabetes are assessed in Chapters 7 and 8.

Chapter 9 provides an overall discussion of the main findings, the strengths and limitations of the thesis, the implications for policy and suggestions for future research.

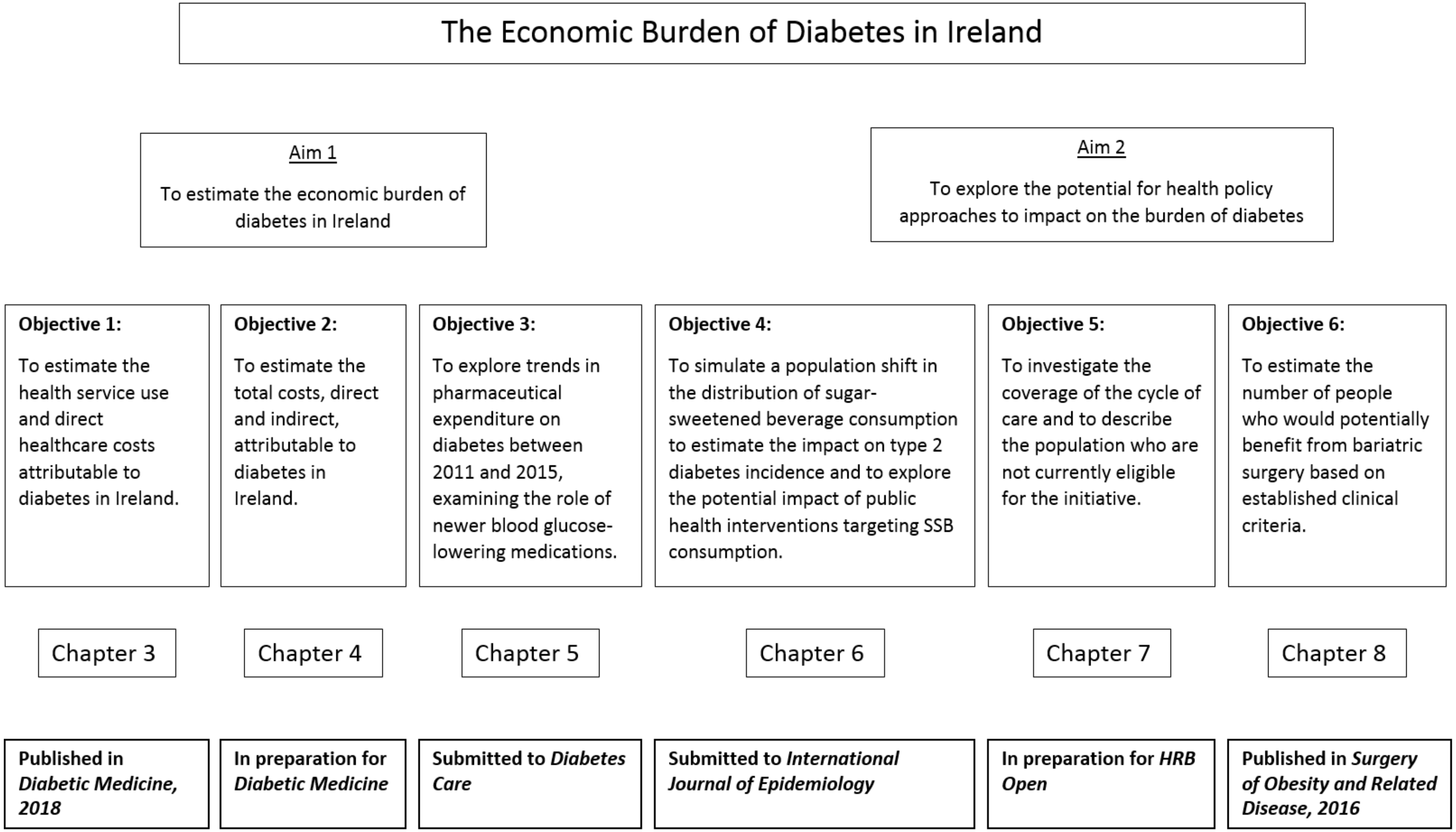


Figure 1.1- Overview of thesis including aims and objectives

2. Background

2.1 Overview

This chapter presents a brief overview of the societal and economic burden of diabetes, both internationally and in Ireland. First, the epidemiology of diabetes and related complications is described, specifically examining recent trends. Second, the economic burden of diabetes is explored and discussed in the context of increasing diabetes prevalence. Third, the implications of the increasing cost of diabetes are outlined with a discussion on prevention approaches to address the burden of diabetes. Finally, three prevention strategies recommended in Irish health policy are presented, namely reducing sugar-sweetened beverage consumption, funding for the structured management of people with type 2 diabetes in primary care and the provision of bariatric surgery.

2.2 Diabetes – a chronic disease

Diabetes is a group of metabolic conditions characterised by hyperglycaemia (27). It results from defects in insulin secretion whereby the pancreas does not produce enough insulin, or from insulin inaction whereby the body cannot effectively use the insulin that is produced, or both. The majority of diabetes cases can be classified into one of two groups; type 1 diabetes or type 2 diabetes (27). It is estimated that five percent of diabetes cases are type 1, while approximately 90% are estimated to be type 2 diabetes (28,29). The remainder of cases include gestational diabetes and other specific types (27). Type 1 diabetes is caused by a deficiency in insulin secretion. The pathogenesis of type 1 diabetes is described as a complex interplay between environmental factors and microbiome, genome, metabolism, and immune systems (30). Type 2 diabetes is characterised by a combination of insulin resistance and an inadequate compensatory insulin secretion response. The causes of type 2 diabetes are better understood than type 1 diabetes, with sedentary lifestyles, physical inactivity, dietary intake and obesity identified as risk factors for the disease (1,31). The long-term complications of diabetes have traditionally been categorised as microvascular and macrovascular complications (32,33). Microvascular complications include retinopathy, neuropathy and nephropathy. Macrovascular complications refer to cardiovascular disease and include coronary heart disease, cerebrovascular disease and peripheral arterial diseases. More recently, diabetes has also been associated with poor cognitive functioning and mental health (34) and some cancers (35,36).

2.3 Global epidemiology of diabetes

The global age-standardised prevalence of diabetes in adults aged over 18 years was estimated at 9.0% (95% CI: 7.2, 11.1) in males and 7.9% (95% CI: 6.4, 9.7) in females in 2014 (4). Using data from 751 population-based surveys and studies, the NCD Risk Factor Collaboration found significant variation in prevalence estimates across world regions. Age-standardised prevalence was lowest in north-western European countries at less than 5% and highest in Polynesia and Micronesia where prevalence was greater than 20%. Between 1980 and 2014, diabetes prevalence increased or at best remained unchanged in all countries worldwide. Over the 35-year period, the number of adults with diabetes increased four-fold reaching an estimated 422 million in 2014 (4). The global increase in numbers of people with diabetes was attributed to population growth and ageing, a rise in age-specific prevalence rates and an interaction of the two. The prevalence of diabetes increases significantly with age (37–39). In high-income countries, diabetes prevalence is highest in those aged 75-79 years and in those aged 60-74 in middle income countries. In low-income countries, diabetes prevalence peaks in the 55-64 age group (40).

The incidence and prevalence of diabetes in the USA doubled between 1980 and 2008, with trends plateauing between 2008 and 2012 (41). Increasing trends in prevalence and incidence in European countries has also been observed, with evidence of stabilising incidence rates in recent years (42–45). In the UK, analysis of primary care data reports a doubling in prevalence of type 2 diabetes between 2000 and 2013 (42). In this population, the incidence of type 2 diabetes also increased over the time period, from 3.69 per 1000 person-years at risk in 2000 to 3.99 per 1000 in 2013 among men and from 3.06 per 1000 to 3.73 among women. However, since 2005 there was some evidence of stabilising incidence rates. One explanation for declining or stabilising incidence rates in the mid to late 2000s is the reduction in the pool of undiagnosed diabetes. In the previous decade, there was an intensification of diagnostic activities (43,44). Despite some evidence of stabilising incidence rates, prevalence increased in all countries over the time periods studied.

2.4 Epidemiology of diabetes in Ireland

In the absence of a diabetes register, data on the epidemiology of diabetes in Ireland is largely from national surveys and pharmacy claims data. Based on data from four nationally representative surveys, the prevalence of diabetes in Ireland is estimated to have increased from 2.2% (95% CI: 1.7, 2.7) of the adult population in 1998 to 5.2% (95% CI: 5.1, 5.3) in 2015 (46). Over this time, there was no significant increase in the prevalence of diabetes in those aged 18-39 years, with prevalence remaining at less than 2%. Among those aged 40-69 years, the prevalence almost doubled in both males and females (3.5% [95% CI: 3.4, 3.6] to 6.6% [95% CI: 6.5, 6.7] and 2.5% [95% CI:2.4, 2.5] to 4.2% [95% CI: 4.1, 4.3], respectively). Similar trends were observed in the 70+ age group, with prevalence increasing from 8.2% (95% CI: 8.0, 8.3) to 15.1% (95% CI: 14.8, 15.2) in males and 4.7 % (95% CI: 4.5, 4.8) to 10.7% (95% CI: 10.5, 10.8%) in females. The prevalence of type 2 diabetes in Irish adults aged over 50 years has been estimated at 8.4% (95% CI: 7.8, 9.0%) (47). Prevalence was higher among males, 10.3% (95% CI: 9.4, 11.2%), than females, 6.6% (95% CI: 5.9, 7.5%). Similar estimates for type

2 diabetes prevalence were published using national pharmacy claims data in Ireland (48). There are no data on trends in incidence rates over time in Ireland.

2.5 Morbidity and mortality

Diabetes is associated with reduced quality of life, morbidity and premature mortality. In 2016, diabetes was the eighth leading cause of years lived with disability globally (49). Much of the burden can been attributed to diabetes-related complications (50).

2.5.1 Morbidity

People with diabetes are at increased risk of developing macrovascular and microvascular complications. The risk of macrovascular complications in people with diabetes is 2-4 times that of the population without diabetes and the risk of microvascular complications is 10-20 times that in people with diabetes compared to those without, even after adjustment for important confounding factors (32,51–53). The prevalence of complications varies greatly between studies due to variations in methods employed, study populations and data sources.

There is a paucity of international data on trends in complications with evidence restricted to a number of high income countries (32). Such evidence suggests that rates of complications have declined over time. Analysis of nationally representative US surveillance data demonstrated, that between 1990 and 2010, rates of lower-extremity amputations, acute myocardial infarction, stroke, end-stage renal disease and death from hypoglycaemic crisis all declined significantly (54). The magnitude of reduction was largest for myocardial infarction with 95.6 fewer cases per 10,000 persons per year (95% CI: 76.6, 114.6), followed by stroke (58.9 fewer cases per 10,000 [95% CI: 41.6, 76.2]). Similar declining trends in cardiovascular event rates in people with diabetes were observed in Canada (55).

While study populations, methods of ascertainment and outcome definitions vary across studies, published data on trends in lower-extremity amputations indicate declining rates over time (32). Lower-extremity amputations have been described as a sentinel outcome for evaluating diabetes care as the risk is influenced by the management of clinical measures including glycaemic control and blood pressure control, lifestyle factors such as tobacco consumption and health system factors such as screening and risk-stratification (56). Rates of lower-extremity amputations in the USA declined by half (51.4%, 95% CI: 68.2, 34.5) between 1990 and 2010 (54), with similar trends observed in European countries and Australia (57–62). Conversely, national trends in rates of lower-extremity amputations in Ireland increased non-significantly between 2004 and 2008 (52). However, trends in major of lower-extremity amputations remained unchanged while minor of lower-extremity amputations rates rose from 96.2 to 127.6 per 100,000 people with diabetes. Minor amputations may reflect improved detection and earlier intervention, consequently preventing the progression from minor to major amputation (52).

Diabetic retinopathy is a leading cause of blindness in working age adults (63–65). The global prevalence of diabetic retinopathy is estimated at 34.6% (95% CI: 34.5, 34.8) among people with diabetes, however estimates are limited by a paucity of data pooled from different study populations, at different time points and with varying methodologies (66). Population-based data from Israel, Scotland, and Germany document reductions in rates of diabetic retinopathy and blindness between the years 1999 and 2010 (65,67,68). Trends in blindness due to diabetic retinopathy among adults aged 18–69 years in Ireland have been published for the years 2004 to 2013 and suggest somewhat similar trends (69). Although there was insufficient evidence to confirm a downward trend, incidence of blindness due to diabetic retinopathy decreased from 31.9 per 100,000 population (95% CI: 21.6, 45.7) in 2004 to 14.9 per 100,000 population (95% CI: 8.2, 25.1) in 2013. The incidence of visual impairment due to diabetic retinopathy increased from 6.4 (95% CI: 2.4, 13.9) per 100,000 in 2004 to 11.7 (95% CI: 5.9, 21.0) per 100,000 in 2013. This may be indicative of local efforts to screen for diabetic retinopathy (69). Since 2013, a national diabetes retinopathy screening programme has been implemented in Ireland (70).

2.5.2 Mortality

Diabetes is one of the leading causes of death worldwide (3). It is associated with excess mortality, with cardiovascular disease being the most common cause of death in people with diabetes (71–76). The Diabetes Atlas Group estimate that in 2013, 5.1 million deaths were attributable to diabetes worldwide, with 619,847 deaths in Europe (77). Diabetes has also been associated with substantial premature mortality from several cancers, infectious diseases, external causes, intentional self-harm, and degenerative disorders (78). International country-level data on trends in mortality are, again, limited to a number of high-income countries and consistently demonstrate reductions in mortality over the past two decades (32,44,54,79,80). All-cause mortality rates and cardiovascular mortality rates in the USA reduced by 23% (95% CI: 10, 35) and 40% (95% CI: 23, 54), respectively, between 1997 and 2006 (79). Similar trends have been observed in Australia between the years 1997-2010 (81). In Europe, reductions in mortality rates have also been observed over similar time periods (43,44,80). Despite this, absolute number of deaths attributable to diabetes worldwide are increasing (3,43). Between 2006 and 2016, absolute number of deaths and the total years of life lost from diabetes rose by 31% (95% UI: 28.9, 33.4) and 25% (95% UI: 23.2, 27.7), respectively (3).

2.6 "Winning the battle but losing the war?"

Declining trends in morbidity and mortality have been more pronounced in populations with diabetes compared to those without, resulting in attenuated relative risks for the associations between diabetes and poor health outcomes and mortality (43,54,79). While such achievements can be attributed to the improvement in risk factor management and processes of care for people with diabetes, the absolute burden of diabetes on society and health systems continues to increase. Declining mortality rates in people with diabetes results in increasing years spent with the condition. The total number of years lived with disability due to diabetes has increased globally between 2006 and 2016 (49). Furthermore, it is estimated that, due to declining mortality rates in the total population, the lifetime probability of developing diabetes has increased for males and females (82,83). Combined with ageing populations and increasing incidence, the absolute numbers of people with diabetes is increasing (4,84). A small increase in incidence of diabetes, observed in the USA between 2000 and 2004, is projected to result in 12 million additional people with diabetes by 2050 (84). Despite declining rates of complications, the increasing numbers of people with diabetes in the population will translate to growing absolute numbers of cases with diabetes-related complications (12,13,32). When trends in diabetes-related complications, such as lower-extremity amputations, are re-assessed with the total population as the denominator less promising trends are evident (13). With significant strides made in the tertiary prevention of diabetes, improvements in population health are being negated by the increasing numbers of people with diabetes (13). With increasing absolute numbers of people with diabetes globally, the societal and economic burden of diabetes is ever more concerning.

2.7 The global economic burden of diabetes

The global economic burden of diabetes was estimated at $1.31 trillion (95% CI: 1.28, 1.36) in 2015, accounting for 1.8% of global Gross Domestic Product (GDP) (5). Substantial variation exists across global regions. The highest absolute economic burden is observed in North America, where the costs of diabetes also account for the highest proportion of GDP (2.6%). Sub-Saharan Africa has the lowest economic burden in absolute terms, while in South Asia the costs of diabetes account for the lowest proportion of GDP (1%) compared to other regions. When grouped by income classification, high-income countries contribute the most to the global economic burden of diabetes with a total of $800 billion spent on diabetes.

A large body of literature has quantified the cost of diabetes at the country level (11,85,86). Cost-of-illness studies estimate the economic burden of a disease with the aim to identify the costs that could potentially be saved if the disease were prevented. These estimates are useful in highlighting the economic burden of diabetes (8,87). Three systematic reviews, published in 2004, 2014 and 2015, document the large and increasing economic burden of diabetes (11,85,86). While the studies identified by Ettaro and colleagues, in 2004, were largely focused on the USA and a small number of high-income European countries, by 2015 there was an emergence of studies from low and middle income countries (11,85). However, comparisons in cost estimates across studies are limited by the wide variation in methodologies employed (11,85,86,88).

2.8 Variation in cost-of-illness methodology

Comprehensive cost-of-illness studies include direct and indirect costs. Incurred by the health system, society, families and the individual patient, direct costs can consist of healthcare costs (for example, health service use, prescription medications and medical supplies) and non-healthcare costs (for example, transportation or any informal care)

(88,89). Indirect costs, incurred by the individual, families, society and employers, estimate the costs of lost productivity associated with a disease (for example, reduced labour force participation and premature mortality). While some studies also include the intangible costs of a disease, using quality of life measures, this category of costs is often omitted due to the difficulty in accurately quantifying quality of life in monetary terms (86). Cost-of-illness studies can be conducted from a variety of different perspectives, determining the costs to be included. The perspectives may measure costs to society, the government, the health care system, private sectors or the individual. Depending on the perspective adopted, cost estimates will vary. A societal perspective is the most comprehensive perspective as it includes all direct and indirect costs (89,90).

2.8.1 Prevalence versus incidence-based approaches

Depending on the epidemiological data used, cost-of-illness studies are either prevalence-based or incidence-based. A prevalence-based approach estimates the economic burden of a disease over a specified period of time, usually a 12-month period or calendar year. This is the most commonly used approach, particularly for chronic conditions with a long duration (88,91). The incidence-based approach calculates the lifetime costs associated with a disease by estimating the number of new cases in a given year, assigning a lifetime cost to each case.

2.8.2 Defining disease associated costs

The costing methodologies for cost-of-illness studies can be classified into two overarching groups; total disease costs and excess costs, and are detailed in **Table 2.1** (11,88). Total disease costs estimate the total healthcare expenditure of people diagnosed with the disease. On the other hand, excess costs identify costs that are attributable to the disease of interest. Within each category, costs can be further categorised by the methodological approach employed. While the aim of the study and data availability will ultimately determine the approach utilised, there are a number of advantages and disadvantages to each approach. The ideal cost-of-illness study will identify the total excess costs independently attributable to diabetes. However, the approach is often restricted by data availability and any cost-of-illness study needs to be tailored to make the best use of the available data.

Table 2.1 – Cost-of-illness methodologies

Methodological Approach	Description	Advantages/disadvantages
<u>Total Costs</u>		
Sum-all medical	Identifies individuals with disease of interest and sums all health expenditure.	- Captures all costs regardless of whether associated with disease or not. - Do not provide useful or meaningful estimates to inform policy. - Can overestimate costs of disease.
Sum-diagnosis specific	Identifies costs relating directly to disease of interest.	- Includes disease-specific expenditure only. - Can underestimate costs, especially for diseases with comorbidities.
<u>Excess Costs</u>		
Disease attributable	Identifies costs using attributable fraction methodology. Identifies the comorbidities caused by the disease of interest and applies population attributable fractions for each comorbidity to aggregate cost data.	- Reliant on robust and appropriately specified attributable fractions. - Can underestimate costs due to inability to capture costs that do not appear directly associated with the disease of interest or where quantifiable associations are not available.
Incremental analysis	Compares excess costs in people with the disease of interest to those without Can be achieved using either a matching or regression-based approach	- Allows for the identification of the excess costs independently attributable to the disease of interest. - Provides policy-relevant estimates. - Dependent on wide range of data availability for people with and without disease of interest

2.9 Cost-of-diabetes studies

The most common method used in cost of diabetes studies is the sum-all medical approach (11). However, by adopting this method, studies capture all healthcare costs regardless of whether they are associated with diabetes or not. Such estimates fail to identify service use that can be attributed diabetes and thus, do not provide useful or meaningful estimates to inform policy. The number of studies estimating the excess costs associated with diabetes has increased in recent years (11,85,86). The disease attributable methodology is also commonly used, although mainly in the USA. This method underestimates service use and costs associated with diabetes due to its inability to capture use that does not appear directly attributable to diabetes (92,93). For instance, mental health co-morbidities in people with diabetes increase health service utilisation (94). Due to its reliance on established quantifiable causal associations, disease-attributable methodology will not capture such excess service use. Furthermore, this method is reliant on robust and appropriately specified population attributable fractions which are not always available.

The use of the incremental cost approach yields the most accurate and policy-relevant estimates of the cost of diabetes as it allows for the identification of the excess costs attributable to the diabetes (11,92,93). This approach allows for the control of important confounding factors and thus the identification of the excess costs independently attributable to diabetes (11,92,93). However, consideration of appropriate covariates is essential. For instance, if the aim is to estimate total excess costs attributable to diabetes adjusting for the presence of macrovascular and microvascular complications will lead to an attenuation in costs and provide an estimate of the costs attributable to diabetes independent of the presence of complications. Few studies have applied the incremental costs approach to examine the cost of diabetes (11). Of the studies adopting this approach, many have focused on specific hospital-based samples or have used routine healthcare data to estimate direct costs. These studies may result in an overrepresentation of people with diabetes and also people with diabetes-related complications. Furthermore, due to data availability constraints, many incremental cost studies control for gender and age only (95). Honeycutt et al. demonstrate that controlling for age and gender only can result in an overestimation of diabetes-related service use and costs (92). Worldwide, there is a lack of accurate, comprehensive and comparable estimates of costs attributable to diabetes (5). Valid and reliable incremental cost estimates for diabetes are required at a regional and country level to improve the accuracy of global cost of diabetes estimates (5,10). To date, the only estimate for the economic burden of diabetes in Ireland comes from the CODEIRE study published in 2006 (96). Using data from 1999/2000, CODIERE uses a sum-all medical approach for a hospital based sample of Irish adults aged over 30 years with diabetes. They do not estimate indirect costs.

Due to wide variations in methodologies, comparisons across studies are hindered (11). However, despite this, there are a number of commonalities across international studies that provide insight into the economic burden of diabetes. Hospital in-patient costs account for the majority of direct expenditure associated with diabetes, followed by medication costs (97–105). Diabetes complications have a substantial impact on both direct and indirect diabetes costs (106–109). The Cost of Diabetes in Europe – Type II (CODE-2) study reported that in patients with both microvascular and macrovascular complications, the total cost of management was increased by 250% compared those without complications (110). More recent estimates are similar. In Denmark, the majority of costs were incurred among patients with major complications in 2011 (106). In Poland, the direct cost of hospital complication treatment were more than five times the direct costs of hospital treatment of people without complications (109). In studies assessing the direct and indirect costs, the ratio between the two varies and with the inclusion of differing cost categories and different methodologies, comparisons are limited. However, it is evident that indirect costs account for a significant proportion of diabetes costs. Global estimates report that 34.7% (95% CI: 34.7, 35.0) of the total economic burden of diabetes is attributable to indirect costs (5). This varied from 40.0% in high-income countries to 33.5% in low-income countries. Higher estimates have been reported in some European countries, with over half the costs attributable to indirect costs in the UK and Poland (107,109).

2.9.1 Rising costs of diabetes

Should previous trends in diabetes prevalence and mortality continue, it is estimated that by 2030, the global economic burden of diabetes will increase to $2.5 trillion (95% CI: 2.4, 2.6) (7). This translates to an increase in costs as a share of global GDP to 2.2%. Major increases in the proportion of GDP attributable to diabetes costs are predicted for all world regions, between 2015 and 2030.

While global projections estimate an inevitable increase in the economic burden of diabetes between 2015 and 2030, country-specific data, demonstrating increasing costs, is only available for a small number of high-income countries (7). Evidence of the increasing cost of diabetes is largely based on research in the USA (8,9,97,107,111). The economic costs of diabetes, calculated by the American Diabetes Association, increased by 26% in the five-year period 2012 to 2017 (8). The increase is driven by increasing numbers of people with diabetes but also rising costs of medical care per person with diabetes (9,97). In the USA, medical spending attributable to diabetes per person doubled between 1987 and 2011 (9). Furthermore, each additional year with diabetes increases annual medical expenditure (112). As mortality rates in people with diabetes decline and years lived with diabetes increase, this has implications for the future costs of diabetes.

Medication costs have been identified as the primary driver of increasing medical expenditure on diabetes (8,9). Over half the increase in medical expenditure is due to rising prescription costs (9). It is suggested that the observed increase in pharmaceutical expenditure can be attributed to a combination of increasing diabetes prevalence, advancements in clinical guidelines advocating long-term glycaemic control and the upsurge of new expensive medical treatments (8–10). As of 2016, there were at new least 171 new drug therapies in development for the treatment and management of diabetes and its related complications (113). With an emphasis on maintaining glycaemic control, the number of classes of glucose-lowering drugs developed over the previous two decades has more than tripled (114). Novel and innovative treatments are expensive and concern has been raised about whether the benefits of these medications outweigh their significantly higher costs (115). While empirical data is scarce, it is predicted these treatments contribute to rising medication costs associated with diabetes and the continued advancement in diabetes-related medical technology will increase per capita medical expenditure per year (9,10,31,116).

2.10 Public health policy response to diabetes

The substantial economic burden of diabetes highlights the urgent need for cost-effective interventions (5). Estimates of the costs of diabetes provide insight into the measures and scale of investment required to address the societal and economic burden of diabetes. Rising medical costs per person with diabetes combined with increasing absolute cases of diabetes highlights the urgent need for cost-effective interventions to efficiently manage diabetes and its complications (12). In tandem with this, the prevention of diabetes is essential to curb the increasing prevalence, ensuring that the future costs of diabetes are curtailed and improvements in rates of morbidity and mortality are realised in economic terms. A multi-level approach is required to tackle the burden of diabetes (14). A public health response to diabetes identifies three areas of prevention required to adequately address the burden of diabetes (10,13–18). Primary prevention employs a population-wide approach with the aim of intervening before a disease occurs. Population based interventions aim to shift the distribution of risk factors in the entire population. Secondary prevention targets those at risk of developing the disease of interest, while tertiary prevention strategies manage and treat the disease once it has manifested with the aim to prevent disease-related complications. Effective interventions for diabetes exist across this continuum of prevention. For diabetes, the most progress has been made in the area of tertiary prevention, evident from the attenuation in relative risks for diabetes-related complications. In terms of preventing the onset of diabetes, attention has focused on the secondary prevention of diabetes in those at high risk or with pre-diabetes (10,13,14,117).

2.10.2 Lessons of the paradox

Despite significant strides made in the tertiary prevention of diabetes, improvements in population health are being negated by the increasing numbers of people with diabetes (13). Unless the incidence is curbed, the absolute numbers of people with diabetes will continue to increase and future costs of diabetes will not be curtailed. The most robust and consistent evidence on cost-effective secondary prevention interventions exists for structured lifestyle interventions and intervention with metformin in those with pre-diabetes (17,118–121). Such interventions have been proven to be clinically effective and cost-effective in reducing diabetes incidence in high risk groups. However, they are limited by the challenges in identifying those in whom the intervention may be beneficial at population level (16,17). The secondary prevention of diabetes through effective structured lifestyle interventions is an essential aspect of intermediate efforts to stabilise diabetes prevalence. However, recent evidence has demonstrated that the impact on diabetes prevalence from this approach alone would be modest and that while they may result in slowing of increasing prevalence rates, the prevalence of diabetes will continue to grow (122,123). Focusing efforts on the secondary prevention of diabetes is essential in the short to intermediate term but a longer-term strategy that widens its focus beyond those with high risk is required (12).

Investment in effective primary prevention interventions is necessary to permanently alter increasing prevalence (122,123). While the 'high risk' approach outlined above aims to protect susceptible individuals, the population approach seeks to control the causes of incidence (124). Diabetes has a long incubation period and is intrinsically linked with sedentary lifestyles, physical inactivity, dietary intake and obesity (1,31). Focusing solely on those with pre-diabetes provides an interim expedient but will alone not stem increasing prevalence (124). An "upstream" or whole population approach shifts the focus from relative risk towards absolute risk, providing opportunities to address the current driving factors of the increasing economic burden of diabetes (14). Population-level interventions consider the role of broader social and environmental risk factors associated with diabetes incidence. However, primary prevention has been described as the weak link in the public health response to diabetes (13).

Hospital inpatient costs and prescription costs are identified as substantial contributors to the economic burden of diabetes and the costs are significantly higher in those with diabetes-related complications (97–105). Tertiary prevention measures aim to reduce diabetes complications and prevent avoidable hospital admissions and therefore have the potential to result in significant cost-savings in the short term.

2.11 Translation into policy and implementation in practice

Valid estimates of the potential impact of public health interventions are essential to allow policy-makers make informed decisions about the cost-benefit trade-off between them. The use of biased designs results in inappropriate policies and confusion among policy-makers, scientists and the public (24). Furthermore, where robust evidence on effective interventions exist, the translation of evidence into policy and the subsequent implementation into practice is not always achieved (117). The impact of interventions is influenced by policy decisions including legislative change, for example, a sugar-sweetened beverage tax and health system changes such as, drug reimbursement decisions or financial reimbursement/remuneration for structured chronic disease management. Although research has provided evidence for preventing or delaying type 2 diabetes, health policy decisions can influence the potential impact on the burden of diabetes (26).

Three effective interventions spanning the prevention continuum have been recommended in recent Irish health policy; one primary prevention strategy and two potential interventions addressing the tertiary prevention of diabetes. The secondary prevention of diabetes, as defined above, has not been addressed in national health policy. Firstly, the primary prevention of diabetes has been addressed in healthy government policy tackling sugar-sweetened beverage consumption. As a substantial body of evidence supports an association between sugar-sweetened beverage consumption and incident type 2 diabetes, population health interventions targeting consumption can potentially play an important role in primary prevention (125). Such interventions have been implemented in numerous countries worldwide, largely in the form of fiscal policies, with the UK and Ireland introducing a tax on sugar-sweetened beverages in April 2018 (19–21). Two effective tertiary prevention interventions have also been recommended; firstly, the provision of funding for structured care for people with type 2 diabetes in primary care through an initiative called the "cycle of care" and secondly, the provision of bariatric surgery (22,23). International consensus now exists that structured management of uncomplicated diabetes in primary care with suitable organisational support constitutes good quality diabetes care. There is growing evidence that primary care led structured diabetes management is associated with improved outcomes for patients (126,127). Integrated diabetes care has been shown to reduce preventable hospitalisations for diabetes-related complications (128). Structured approaches to diabetes care demonstrate improvements in glycaemic control and cardiovascular risk factors (129,130). Similarly, the clinical and cost-effectiveness of bariatric surgery makes it another important tertiary prevention option for diabetes (131). Bariatric surgery is associated with reductions in the use of medications and in overall health care costs in patients with type 2 diabetes (132). However, for these policies to have meaningful impacts on the burden of diabetes in Ireland, the translation of evidence into policy and the implementation into practice essential.

2.12 Summary

Diabetes places a substantial burden on health systems and national economies (5). With the absolute numbers of diabetes cases increasing globally and evidence of rising medical expenditure per person with diabetes, the growth in economic burden will continue in coming years (4,7,9). Cost-of-illness estimates quantify the economic burden of diabetes and identify potential areas of cost-saving. They are used to inform and motivate policy-makers to address the burden of disease.

There is wide variation in the methodological approaches employed to estimate the costs of diabetes (11). Worldwide, there is a lack of accurate, comprehensive and comparable estimates of costs attributable to diabetes (5). The most recent estimates of the economic burden of diabetes in Ireland are from 1999/2000 and are limited to the direct hospital costs in people with diabetes (96). Chapters three and four will provide recent, comprehensive and robust estimates of the costs of diabetes in Ireland.

Hospital costs and prescription costs account for the vast majority of the direct costs of diabetes. Medication costs have been identified as the primary driver of increasing medical expenditure on diabetes (8,9), with over half the increase in medical expenditure due to rising prescription costs (9). Chapter five of this thesis will explore trends in prescription costs in Ireland and in particular assess the impact of novel blood glucose-lowering treatments on expenditure.

The increasing economic burden of diabetes and trends in the descriptive epidemiology of diabetes have important implications for health policies aiming to address the burden. Effective interventions across the prevention continuum are necessary with primary, secondary and tertiary prevention playing important roles in addressing the different facets of the epidemic. Furthermore, although research has provided evidence for preventing or delaying type 2 diabetes, health policies determine their potential impact on the burden of diabetes (26).

Three effective interventions spanning the prevention continuum have been recommended in recent Irish health policy; a sugar-sweetened beverage levy, dedicated remuneration for structured care for type 2 diabetes in primary care and the provision of bariatric surgery. Chapter six will explore the potential impact of the recently introduced sugar-sweetened beverage levy in curbing type 2 diabetes incidence in Ireland. Chapters seven and eight explore the potential for structured care for type 2 diabetes in primary care and the provision of bariatric surgery to reduce the burden of diabetes in Ireland, as provided for in Irish health policy.

3. Health Service Utilisation and Related Costs Attributable to Diabetes

3.1 Abstract

Introduction

Worldwide, there is a lack of accurate, comprehensive and comparable estimates of the health service use and costs associated with diabetes. This study aims to estimate the health service use and direct healthcare costs attributable to diabetes using best available data and methods.

Methods

A nationally representative sample of adults aged ≥50 years was analysed (n=8,107). Health service use in the previous 12-months included the number of General Practitioner (GP) visits, out-patient department visits, hospital admissions, and Accident and Emergency (A&E) attendances. Multivariable negative binomial regression estimated associations between diabetes and frequency of visits. Average marginal effects were applied to unit costs for each health service and extrapolated to the total population, calculating the incremental costs associated with diabetes.

Results

The prevalence of diabetes was 8.0% (95% CI:7.4%, 8.6%). In fully adjusted models, diabetes was associated with additional health service use. Compared to those without diabetes, people with diabetes have on average 1.49 (95% CI:1.10, 1.88) additional GP visits annually. Diabetes was associated with an 87% increase in out-patient visits, 52% increase in hospital admissions and 33% increase in A&E attendances ($p<0.001$). The incremental cost of this additional service use, nationally, is an estimated €88,894,421 annually, with hospital admissions accounting for 67% of these costs.

Conclusion

Using robust methods, we identify substantial increased service use attributable to diabetes across the health system. Our findings demonstrate the urgent need to invest in the prevention and management of diabetes.

3.2 Introduction

The number of people with diabetes has increased four-fold in the past 35 years and it is now the seventh leading cause of years lived with disability worldwide (2,4). The impact of diabetes on health systems and national economies is of growing concern. In 2015, the global cost of diabetes was estimated to be US$1.31 trillion, with direct medical costs accounting for two thirds of the costs (5). Increasing prevalence combined with rising per capita medical expenditure indicate that the burden of diabetes on health systems will continue to escalate (9). An understanding of the health service use and related costs associated with diabetes is necessary to inform national policies and the allocation of scarce resources. It is also essential in identifying and evaluating methods of cost saving.

Worldwide, there is a lack of accurate, comprehensive and comparable estimates of the health service use and costs attributable to diabetes (5). This is largely due to the variation in methodologies employed (11). Furthermore, the approach used affects the policy relevance of the estimates. There are three main methodological approaches; sum-all medical approach, disease-attributable approach and incremental cost analysis. The most common method applied for estimating cost of diabetes is the sum-all medical approach (11). This method fails to identify service use attributable to diabetes and thus, does not identify costs that can be avoided by diabetes prevention or management interventions. As a result, the sum-all medical approach does not provide meaningful estimates to inform policy decisions. Another common method used is the disease-attributable approach, whereby attributable fractions for conditions associated with diabetes are applied to health service use data to identify the proportion attributable to diabetes (11). This method underestimates service use and costs associated with diabetes due to its inability to capture use that does not appear directly attributable to diabetes (11,92). For instance, mental health co-morbidities in people with diabetes increase health service utilisation (94).

However, due to its reliance on established quantifiable causal associations, disease-attributable methodology will not capture such excess service use.

More recent studies adopt an incremental costing approach. This method identifies the incremental health service use and costs for people with diabetes compared to those without, therefore capturing all costs associated with diabetes. The incremental costing approach also allows for consideration of other factors known to influence health service use including age, sex, ethnicity, education, socio-economic status, health status and lifestyle factors (133). Thus, it is possible to estimate health service use that is independently associated with diabetes (92,112). To provide more precise estimates of the global cost of diabetes, there is an urgent need for valid and reliable country-level data (5). This study aims to provide robust estimates of health service use and direct healthcare costs attributable to diabetes, from a societal perspective, by applying an incremental cost approach with appropriate adjustment using a nationally representative sample of a community-dwelling adults, aged 50 years and over, with and without diabetes.

3.3 Methods

Study design

A cross-sectional analysis of data from the first wave of The Irish Longitudinal Study of Ageing (TILDA) was conducted. TILDA is a nationally representative prospective cohort study of community-dwelling adults aged 50 years and over in the Republic of Ireland (134). The sampling frame used for TILDA was the Irish Geodirectory, a comprehensive and up-to-date list of all residential addresses in Ireland. A multistage probability sampling design was used, with each residential address in the country having an equal probability of selection (134). Eligible addresses were defined as any household with a person aged ≥50 years. All household residents aged ≥50 years were eligible to participate in the study. The estimated number of eligible households was 10,129. Of these, 6,282 households participated (response rate 62%) and 8,175 individuals were recruited. Ethical approval was obtained from Trinity College Dublin Research Ethics Committee.

Data Collection

Data collection occurred between October 2009 and November 2011. Participants were visited in their home by trained interviewers who used computer-assisted personal interviewing (CAPI). This included detailed questions about socio-demographics, physical and mental health, self-reported doctor-diagnosis of chronic conditions and health service use.

Variable definition

The outcome of interest was self-reported health service use. Participants were asked about the frequency of visits to General Practitioner (GP) services, outpatient department visits, hospital admissions and Accident and Emergency (A&E) attendances in the past 12 months. They were also asked whether they had attended any of the following ancillary state services in the 12 months preceding the survey; dietician, chiropody, optician, public health or community nurse, or psychology/counselling services. Individuals were classified as having diabetes if they self-reported a previous doctor-diagnosis of diabetes. To distinguish between people with type 1 and type 2 diabetes, we defined those who were aged less than 50 years at diabetes diagnosis and reported injecting insulin, but not taking oral hypoglycaemic agents, as having type 1 diabetes. All others were classified as having type 2 diabetes. Participants who reported a doctor-diagnosis of diabetes during the CAPI were asked the question ‘Has a doctor ever told you that you have any of the following conditions related to your diabetes?'. The conditions listed were: leg ulcer, protein in urine, lack of feeling and tingling pain in legs and feet due to nerve damage, damage to the back of your eye. Any participant who answered yes to any of the above was considered to have a microvascular complication. Any participant who self-reported a doctor diagnosis of heart attack (myocardial infarction), heart failure (congestive cardiac failure), stroke (cerebrovascular accident) and mini stroke (transient ischaemic attack) were considered to have macrovascular complications. Other variables of interest included age (in years), gender, marital status (yes/no), education (primary, secondary, third level), location (urban/rural), healthcare cover (means tested public health insurance, private health insurance, both, neither), self-reported health status (excellent, very good, good, fair, poor) and other chronic conditions deemed not to be associated with diabetes. These conditions were lung disease, asthma, arthritis, osteoporosis, cancer, Parkinson's disease and peptic ulcer disease.

Statistical analysis

Health service utilisation was compared across populations with and without diabetes. The differences in the proportion of people attending each health service was analysed using Pearson's chi-square test. Independent samples t-test was used to analyse the difference in the mean number of visits to each service. Logistic regression was used to model the association between diabetes and attendance at ancillary state services. Negative binomial regression models were used to analyse the association between diabetes and the frequency of health service use. Poisson, negative binomial, zero-inflated Poisson and zero-inflated negative binomial regression models were explored. Model selection was informed by Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) statistics and by comparing predicted and observed probabilities, with negative binomial regression being selected as the most appropriate model (Supporting Information, Appendix 1) (135). Average marginal effects were calculated, providing an estimate of the excess number of visits/admissions attributable to diabetes on average. The average marginal effects were computed using the post-estimation command, *margins dydx*, in Stata. This calculates a predicted probability for each case with the fixed and observed values of variables, and then averages the predicted values (136).

The Anderson framework for the societal and individual determinants of health care utilisation was used to inform the selection of appropriate variables to include in the multivariable regression models, with the aim of identifying the independent effect of diabetes on health service use (137). The Anderson framework categorises determinants as either predisposing, enabling or need factors. Any variables that could potentially mediate the association between diabetes and health service use were omitted. Multivariable regression was used to first adjust for predisposing factors (age, gender and marital status), then enabling factors (education, healthcare cover and location) and finally need factors (other chronic conditions).

Sampling weights were applied to all data analyses to adjust for differential non-response and to reduce the potential for participation or selection bias (134). Complete data was available for 99.1% of the sample and so a complete case analysis was carried out. Analysis was carried out in Stata v.12 for windows (StataCorp, College Station, TX, USA) using the survey function (svy).

Calculation of costs

The average marginal effects for significant associations were applied to unit costs for the relevant health service. A societal perspective was adopted, applying average unit costs of €50 for a GP visit, €160 for an out-patient department visit, €5,030 for a hospital in-patient admission and €183 for an A&E attendance previously calculated for Ireland (138,139). These costs were extrapolated to the total population with diabetes to calculate the incremental health service costs. The total population with diabetes was estimated by applying the prevalence of diabetes in the sample to the most recent Irish census figures (2016). Cost estimates are reported in Euro and US dollars (USD) and were inflated to represent costs for 2016 using the Consumer Price Index (CPI) Inflation Calculator for Ireland (140). To reflect uncertainty in the estimates of average unit costs, a sensitivity analysis was conducted whereby these estimates were varied by +/- 20% (141).

3.4 Results

Of the 8,107 participants included in the analysis, 51.9% were female and 41.5% were aged 65 years or older. The prevalence of diabetes was 8.0% (95% CI: 7.4, 8.6), only 11 participants had type 1 diabetes. Among people with diabetes, 15.8% (95% CI: 13.0, 19.2) reported a macrovascular complication, while 26.3% (95% CI: 22.7, 30.3) reported a microvascular complication.

There were significant differences between the population with and without diabetes (**Table 3.1**). People with diabetes were older, had a lower proportion of females, lower levels of educational attainment and lower self-reported health status. They were also more likely to be covered by public health insurance. There was significantly higher service utilisation among people with diabetes for all health services, except psychology/counselling services. Those with diabetes reported an average of 5.8 GP visits in the past 12 months compared to 3.8 visits among those without diabetes ($p<0.001$). 60.8% (95% CI: 56.7, 64.8) of people with diabetes reported attending an out-patient department in the last year compared to 39.1% (95% CI: 37.7, 40.5) of people without diabetes. A higher proportion of people with diabetes also reported being admitted to hospital in the previous 12 months (19.8%, 95% CI: 16.7, 23.2) than those without diabetes (12.4%, 95% CI: 11.6, 13.2). Similar variations were observed for A&E attendances, with 20.5% (95% CI: 17.3, 24.1) of people with diabetes attending A&E compared to 14.9% (95% CI: 14.0, 15.8) of people without.

Table 3.1 - Characteristics of population by diabetes diagnosis

	Population without diabetes % (n=7486)	Population with diabetes % (n=621)	P value
Female	53	42	<0.001
Age			
50-64	60	44	
65-74	23	32	
75+	17	25	<0.001
Rural residence	44	40	0.12
Married	66	63	0.11
Education			
None/primary	37	50	
Secondary	44	37	
Third level	19	13	<0.001
Health care cover			
Medical card	35	50	
Private health insurance only	38	25	
Dual cover	16	19	
No cover	11	7	<0.001
Diabetes-related condition			
Macro vascular	8	16	<0.001
Micro vascular	-	26	
Other chronic illness*	47	51	0.07
Self-reported health			
Excellent/very good	55	33	
Good	30	32	
Fair/poor	15	36	<0.001
GP visits			
Attended past year	87	96	<0.001
Mean (SD) no. visits past year	3.8 (4.1)	5.8 (5.1)	<0.001
Outpatient department			
Attended past year	39	61	<0.001
Mean (SD) no. visits past year	1.1 (2.1)	2.2 (2.7)	<0.001
Hospital admissions			
Admitted in past year	12	20	<0.001
Mean (SD) no. admissions past year	0.2 (0.6)	0.3 (.08)	<0.001
A&E attendance			
Attended in past year	15	21	<0.001
Mean (SD) no. visits past year	0.2 (0.7)	0.3 (0.8)	0.01

Access to ancillary state service	0.6	11	<0.001
Dietician	4	16	<0.001
Chiropody services	12	21	<0.001
Optician	6	12	<0.001
Public health/community nurse	0.8	1.2	0.40
Psychology/counselling services			

*lung disease, asthma, arthritis, osteoporosis, cancer, Parkinson's disease and peptic ulcer disease

There were large statistically significant differences in the proportion of people attending all ancillary state services in the previous year between the two populations, other than attendance at a psychologist or counsellor (**Table 3.1**). The proportion of people with diabetes attending these services did not exceed 21%. **Table 3.2** documents the adjusted odds ratios for attending ancillary state services for people with diabetes compared to those without. The odds of people with diabetes attending a dietician were 19.2 times that of the odds in people without diabetes (95% CI: 12.4, 29.6). People with diabetes were 4 times more likely to attend a chiropodist than those without (95% CI: 3.0, 5.5). Diabetes was also significantly associated with an approximately 60% increased odds of attendance at an optician or public health nurse, with odds ratios of 1.58 (95% CI: 1.27, 1.96) and 1.57 (95% CI: 1.17, 2.10), respectively.

Table 3.2 - Adjusted odds ratios for the association between diabetes diagnosis and ancillary service use in previous 12-month period

Ancillary service	Adjusted odds ratio (95% CI)[1]	P-value
Dietician	19.2 (12.4, 29.6)	<0.001
Chiropody	4.06 (3.00, 5.50)	<0.001
Optician	1.58 (1.27, 1.96)	<0.001
Public health/community nurse	1.57 (1.17, 2.10)	0.003
Psychology/counselling service	1.47 (0.66, 3.27)	0.34

[1]Models adjusted for age, gender, marital status, urban/rural location, education, healthcare cover, chronic conditions.

The incidence rate ratio (IRR) and average marginal effects (AME) from the multivariable negative binomial regression models are presented in **Table 3.3**. There were statistically significant positive associations between diabetes and the frequency of GP visits, out-patient department visits, hospital admissions and A&E attendances. Adjustment for important confounding variables resulted in an attenuation of the IRR point estimates. In the fully adjusted models, people with diabetes had a higher rate of GP visits with an IRR of 1.39 (95% CI:1.29, 1.50). A similar pattern was observed for out-patient department visits and hospital admissions. Diabetes was associated with an 87% increase in out-patient department visits and a 52% increase in hospital admissions ($p<0.001$). A&E attendance was also associated with diabetes (IRR: 1.33; 95% CI:1.06, 1.66). On average, 1.49 (95% CI:1.10, 1.88) additional GP visits were attributable to diabetes in a 12-month period and approximately one additional out-patient visit (0.97; 95% CI:0.73, 1.21).

Table 3.3 - Multivariable negative binomial regression results

Health service	Model 1 – Crude		Model 2 - Predisposing		Model 3 - Enabling		Model 4 - Need	
	IRR	**AME**	**IRR**	**AME**	**IRR**	**AME**	**IRR**	**AME**
GP visits	1.53 (1.42, 1.64) p<0.001	1.99 (1.58, 2.40) p<0.001	1.50 (1.38, 1.62) p<0.001	1.88 (1.45, 2.32) p<0.001	1.38 (1.28, 1.49) p<0.001	1.46 (1.08, 1.84) p<0.001	1.39 (1.29, 1.50) p<0.001	1.49 (1.10, 1.88) p<0.001
Outpatient department	1.93 (1.73, 2.17) p<0.001	1.04 (0.81, 1.27) p<0.001	1.91 (1.70, 2.14) p<0.001	1.01 (0.79, 1.24) p<0.001	1.77 (1.58, 1.99) p<0.001	0.87 (0.65, 1.08) p<0.001	1.87 (1.65, 2.11) p<0.001	0.97 (0.73, 1.21) p<0.001
Hospital admission	1.68 (1.35, 2.09) p<0.001	0.12 (0.06, 0.19) p<0.001	1.58 (1.26, 1.98) p<0.001	0.11 (0.04, 0.17) p=0.001	1.49 (1.20, 1.85) p<0.001	0.09 (0.03, 0.15) p=0.002	1.52 (1.21, 1.91) p<0.001	0.10 (0.03, 0.16) p=0.002
A&E attendance	1.42 (1.15, 1.77) p=0.001	0.09 (0.03, 0.16) p=0.006	1.41 (1.13, 1.77) p=0.002	0.09 (0.02, 0.16) p=0.008	1.34 (1.07, 1.68) p=0.01	0.08 (0.01, 0.14) p=0.02	1.33 (1.06, 1.66) p=0.01	0.07 (0.01, 0.14) p=0.03

IRR – Incidence Rate Ratio, AME – Average Marginal Effect

Model 1 – crude association

Model 2 – adjusted for age, gender, marital status

Model 3 – adjusted for age, gender, marital status, education, healthcare cover, location

Model 4 – adjusted for age, gender, marital status, education, healthcare cover, location, chronic conditions.

The population-based cost estimates for the incremental health service use associated with diabetes are presented in **Table 3.4**. The total population in Ireland in 2016, aged 50 years or over, was 1,446,460. The prevalence of diabetes in this sample was applied, estimating that 115,717 adults aged 50 years or over have diabetes, in Ireland. The incremental health service use associated with diabetes is estimated to cost €88,894,421 per annum. Hospital admissions account for the majority of this spending, costing an estimated €60,002,517. The results of the sensitivity analysis are displayed in **Table 3.5**. By varying the unit cost estimates by +/- 20%, the cost of the incremental health service use associated with diabetes fluctuates from €71,115,537 to €106,673,305.

Table 3.4 – Total incremental health service costs attributable to diabetes

Health service	**Direct costs (95% Confidence Interval)**	
	Euro	**USD**
GP visits	8,886,425 (6,560,448 – 11,212,403)	10,358,107 (7,645,924 – 13,069,288)
Out-patient department visits	18,512,617 (13,932,175 – 23,093,058)	21,578,491 (16,239,483 – 26,917,499)
Hospital admissions	60,002,517 (18,000,755 – 96,004,027)	69,939,533 (20,981,860 – 111,903,253)
A&E attendances	1,492,862 (213,266 – 2,985,725)	1,740,095 (248,585 - 3,480,191)
Total	88,894,421 (38,706,645 – 133,295,212)	103,616,226 (45,116,852 – 155,370,232)

USD – United States Dollars

Table 3.5 – Sensitivity analysis - total incremental health service costs attributable to diabetes

Health service	Direct costs, € (95% Confidence Interval) -20%	+20%
GP visits	7,109,140 (5,248,359, 8,969,922)	10,663,710 (7,872,538, 13,454,883)
Out-patient department visits	14,810,093 (11,145,740, 18,474,446)	22,215,140 (16,718,612, 27,711,669)
Hospital admissions	48,002,013 (14,400,604, 76,803,221)	72,003,020 (21,600,906, 115,204,832)
A&E attendances	1,194,290 (170,613, 2,388,580)	1,791,435 (255,919, 3,582,870)
Total	71,115,537 (30,965,316, 106,636,169)	106,673,305 (46,447,974, 159,954,254)

3.5 Discussion

Using a large nationally-representative population based study, we provide robust estimates of health service use and related costs attributable to diabetes. We identify substantial increased service use associated with diabetes across the health system. Due to the high costs of hospital admissions, hospitalisation costs place the largest burden on the health service accounting for more than two thirds of the total costs attributable to diabetes.

Diabetes was associated with a 39% increase in GP visits and an 87% increase in out-patient department visits. This translated to an additional 1.49 GP visits on average per annum and approximately one additional out-patient visit. Due to the higher unit cost of out-patient visits, the associated costs are more than twice that of primary care costs. With ageing populations and the increasing burden of chronic disease, greater attention has been paid to coordinating patient care according to levels of disease complexity. There has been a shift towards multidisciplinary shared management of complex cases of diabetes across primary and secondary care settings, and structured management of people with uncomplicated diabetes in primary care with suitable organisational support (142). These findings suggest this shift in routine care settings could result in considerable cost savings.

Diabetes diagnosis was associated with increased hospital admissions, in line with a number of international studies that document higher rates of hospitalisations in people with diabetes (143,144). While many studies only take age and gender into consideration, our findings add to the literature by indicating that, in a population based sample, diabetes remains associated with increased hospital admissions after controlling for a wide range of important potential confounders. Our analysis shows that diabetes was associated with a 52% increase in admissions. Due to variations in study populations and methodological approaches, direct comparisons with previous studies are limited. One study conducted in Tayside, Scotland, reported a 100% increase in rates of hospital admissions in people with diabetes compared to those without (145). This is a crude estimate and the study population was significantly younger.

Almost 70% of the health service costs associated with diabetes resulted from hospital admissions. Numerous studies report hospital admissions as the main driver of costs associated with diabetes and our findings highlight the need to provide effective interventions for the management of diabetes and related complications (97,99). Increased risk of hospitalisation in people with diabetes is attributable to macrovascular and microvascular complications (100,143). While significantly higher than the population without diabetes, it is concerning that less than a quarter of people with diabetes reported attending ancillary state services such as chiropody and dietetic services. A shortage of allied health professionals has previously been identified as a barrier to delivering diabetes care in

Ireland (146). International guidelines identify these services as part of routine care for people with diabetes (147). Such services, specifically foot care services and dietetic interventions for people with diabetes, are effective in preventing complications and subsequently reducing healthcare expenditure (148). While these services may be available privately, at a significant cost to the patient, it is imperative that such effective services are accessible to all people with diabetes.

Addressing many of the limitations of previous studies, we provide robust estimates of health service utilisation attributable to diabetes. By adopting an incremental approach, we ensure that any excess health service use attributable to diabetes is identified, not just the service use that appears directly related to diabetes. For instance, this approach ensures that excess service use associated with mental health issues is captured in our results. A nationally-representative sample provides an appropriate comparison group to calculate incremental use and costs, avoiding the overrepresentation of people with diabetes and diabetes-related complications. To date, studies have largely relied on hospital-based samples or administrative healthcare data (11). Unlike much of the existing literature on the cost of diabetes, we specifically address the issue of endogeneity (11). Our study accounts for important confounding variables that have previously been recognised as predictors of service use, identifying the costs that can be independently attributed to diabetes (133). The adjustment for such factors led to the attenuation of our estimates. Most incremental studies control for gender and age only due to data availability constraints (5,11,100,104), and so may overestimate service use and costs attributable to diabetes. Furthermore, any variables identified as potential mediating factors were omitted from the analyses ensuring that the findings were not an underestimation of the true association between diabetes and health service use. To date, the only nationally representative studies adopting the incremental costing approach and adjusting for additional factors were conducted in the USA (9,112).

While we cannot infer causality due to the cross-sectional nature of the data, almost 90% of the cohort had attended the GP in the previous year. Thus, the potential for reverse causality whereby those who attend the GP are more likely to be diagnosed with diabetes and diabetes-related complications is reduced. Furthermore, less than one percent of the cohort had undiagnosed diabetes on the basis of HbA1c measurement (149). While the reliance on self-report doctor diagnoses may potentially introduce misclassification bias and result in inaccurate estimates, evidence demonstrates that self-report is a suitable measure for estimating the prevalence of chronic conditions including diabetes when compared to medical records (150). Health service utilisation is also based on self-report introducing potential for measurement bias. However, recent studies suggest there is no evidence of differential recall bias according to demographics or health status (151). This method is widely used in health services research. The data were weighted to adjust for differential non-response with the aim to minimise the potential for selection bias and improve the representativeness of the findings. However, our estimates are only representative of the excess health service use and costs associated with diabetes in community-dwelling adults aged 50 years and older and so do not represent costs for the total population. It is estimated that less than 1.6% of the adult population aged 50 years and older in Ireland are in long-term residential care (152). It is also important to note that cost estimates are based on average unit costs per visit/admission. Diabetes-related admissions are more expensive and as a result our cost estimates are likely to be an underestimation of the true costs of hospital admissions (99). The cost estimates also only refer to additional service use for GP and hospital services. Due to data limitations, we were unable to calculate the costs associated with ancillary service use or community care. Although we employ a societal perspective in calculating the associated costs, our estimates represent the direct medical costs and do not consider the indirect costs associated with excess health service use. The accuracy of our estimates could be improved in further research by applying the demonstrated methods to individual level cost data. The challenge, however, is to find a data source with all necessary information. In the absence of a unique identifier in Ireland, this was not possible.

In conclusion, our findings demonstrate that diabetes is associated with substantial additional health service use and costs, with hospital admissions accounting for more than two thirds of the cost burden. We highlight areas for potential cost-savings in the context of finite healthcare resources, such as a shift in routine management to primary care and improved access to effective ancillary services such as foot care services and dietetic interventions (148). We provide robust informative estimates for policy-makers by identifying additional health service use and costs that are attributable to diabetes. Effective interventions aimed specifically at both diabetes prevention and management therefore have the potential to directly impact on these health care costs. The challenge is to identify cost-effective interventions, examine the trade-offs between them and determine how to best implement them.

7. Cycle of Care for people with diabetes: an equitable initiative?

7.1 Abstract

Introduction

In 2015, the diabetes “cycle of care” was launched. This national initiative financially remunerates General Practitioners for structured care for people with type 2 diabetes. However, eligibility for the scheme is limited to those with means-tested public health insurance. We aim to investigate the coverage of the cycle of care and to describe the socio-demographic and clinical profile of the population who are not currently eligible.

Methods

Cross-sectional analysis of wave one (2009-2011) of The Irish LongituDinal study on Ageing (TILDA). Individuals were classified as having type 2 diabetes if they self-reported a previous doctor diagnosis or if they reported the use of oral hypoglycaemic agents. Estimates were applied to the 2016 census figures estimating absolute population eligible/non-eligible for the scheme. Pearson’s chi-square test was used for the comparison of categorical variables across eligibility status while Independent samples t-test was used for continuous data.

Results

Of the 8,107 TILDA participants, 609 had type 2 diabetes (prevalence: 7.9% [95% CI: 7.3%, 8.5%]). While the majority of people aged over 50 years with type 2 diabetes are covered by the cycle of care, 31.6% (95% CI: 27.8, 35.6) are not eligible for the scheme, equating to 36,567 (95% CI: 32,170, 41,196) individuals with type 2 diabetes. People not eligible were less likely to be on insulin and more likely to be managing their diabetes without medication.

Conclusion

A third of people over 50 years of age, with type 2 diabetes, are not eligible for the cycle of care. Current eligibility criteria for the cycle of care does not identity people on the basis of clinical need but rather on income.

7.2 Introduction

With rising prevalence and burgeoning healthcare costs, diabetes embodies many of the challenges facing health systems. The prevalence of doctor diagnosed diabetes in Ireland has increased from 2.2% of the adult population in 1998 to 5.2% in 2015 (46). In adults aged 50 years and older, the prevalence of type 2 diabetes is 8.5% (47). Healthcare costs attributable to diabetes in those aged over 50 years are estimated at €89 million per annum with hospital admissions accounting for almost 70% of costs (153). Out-patient department visits attributable to diabetes cost an estimated €18.5 million per annum.

International consensus now exists that structured management of uncomplicated diabetes in primary care with suitable organisational support constitutes good quality diabetes care. There is growing evidence that primary care led structured diabetes management is associated with improved outcomes for patients (126,127). Recent guidance on integrated care for diabetes in Ireland recommends that patients with uncomplicated type 2 diabetes are to be managed in primary care and patients with complicated type 2 diabetes managed between primary and secondary care (22). The management of type 1 diabetes remains in secondary care. Uncomplicated patients are defined as patients not on insulin but treated by diet or glucose lowering agents only, controlled HbA1c and no diabetes-related complications (22).

In 2015, the diabetes "cycle of care" was launched. This is the first national initiative to financially remunerate General Practitioners (GPs) for providing structured care for people with type 2 diabetes. GPs are remunerated for providing two structured diabetes review visits per year. The initiative also establishes formal requirements for registering, recording and reporting processes of care. However, GPs will only be remunerated for patients entitled to the General Medical Services scheme or the GP-visit scheme. Eligibility for these schemes is means-tested. We aim to investigate the coverage of the cycle of care and to describe the population who are not currently eligible for the initiative.

7.3 Methods

A cross-sectional analysis of wave one (2009-2011) of The Irish LongituDinal study on Ageing (TILDA) was conducted. TILDA is a population-based prospective cohort study of community-dwelling adults aged 50 years and over (231). The sampling frame is the Irish Geodirectory, which is a comprehensive and up-to-date list of all residential addresses in Ireland. A multistage probability sampling design was used. Participants completed a computer-assisted personal interview (CAPI). Individuals were classified as having diabetes if they self-reported a previous doctor diagnosis or if they reported the use of oral hypoglycaemic agents. Type 1 diabetes was defined as those who were aged less than 50 years at diabetes diagnosis and reported injecting insulin, but not taking oral hypoglycaemic agents. All others were classified as having type 2 diabetes. Participants who reported a doctor diagnosis of diabetes during the CAPI were asked the question ‘Has a doctor ever told you that you have any of the following conditions related to your diabetes?’. The conditions listed were: leg ulcer (peripheral vascular disease), protein in urine (served as a proxy for elevated urine albumin creatinine ratio), lack of feeling and tingling pain in legs and feet due to nerve damage (diabetic neuropathy), damage to the back of your eye (diabetic retinopathy). These were defined as microvascular complications. Participants were considered as having a macrovascular complication if they self-reported a doctor-diagnosis of any of the following; heart attack (myocardial infarction), heart failure (congestive cardiac failure), stroke (cerebrovascular accident) or mini stroke (transient ischaemic attack). During the CAPI, participants were also asked about their health cover. People who reported either having a medical card or a doctor-visit card are eligible for the cycle of care. Self-reported health service use in the previous 12 months included number of GP visits, out-patient department visits, hospital admissions and attendance at ancillary services.

Pearson's chi-square test was used for the comparison of categorical variables across eligibility status while independent samples t-test was used for continuous data. The proportion of people who are eligible for the cycle of care was applied to the most recent census figures (2016) to estimate the absolute numbers of people covered and not covered by the scheme. Survey weights were applied to the analysis to reflect the complex sampling design and to adjust for participation bias (134). Analysis was carried out in Stata v. 12 for windows (StataCorp, College Station, TX, USA) using the survey function (svy).

7.4 Results

A total of 8,175 participants from 6,282 households completed the CAPI (response rate: 62%). Of these, 8,107 had complete data and were included in the analysis. Almost 70% of people with type 2 diabetes, aged 50 years and over, are covered by the cycle of care (**Table 7.1**). However, 31.6% (95% CI: 27.8-35.6) of people are not eligible for the scheme. In 2016, we estimate that 36,567 people, aged 50 years and over, were not eligible for the cycle of care scheme.

Table 7.1 - Cycle of Care eligibility

Cycle of Care	% (95% CI)	Population Estimate 2016 N (95% CI)
Eligible	68.5 (64.4, 72.2)	79,267 (74,523, 83,548)
Non-eligible	31.6 (27.8, 35.6)	36,567 (32,170, 41,196)

Table 7.2 shows the characteristics of the population eligible for the cycle of care and those not eligible. There was a significantly higher proportion of females in the eligible population compared to those not covered by the scheme. The age breakdown between the groups also differed. Those eligible for the cycle of care were older with 34.2% aged over 75 years compared to only 4.1% of those not eligible. A quarter of people not eligible under the cycle of care had completed third level education, compared to just 7.4% of those who were eligible. The proportion of people living in urban locations did not differ significantly between the groups. While a higher proportion of the eligible population reported fair or poor health, this was not statistically significant. Similarly, were no significant differences in the prevalence of diabetes complications between the groups. There were significant differences, however, in diabetes treatment. Among those eligible for the cycle of care, 17.4% were on insulin compared to 9.8% of people not eligible. A significantly higher proportion of non-eligible people reported no medical treatment for their diabetes (27.4% compared to 14.7%).

Those eligible for the cycle of care reported a mean number of 6.7 GP visits in the past 12 months, compared with 3.8 visits in the those not eligible ($p<0.001$). There was no significant difference in the proportion of people attending outpatient departments in the previous 12 months between the two groups ($p=0.36$). The mean number of visits to an outpatient department per 12 months was 2.4 in the eligible group and 1.6 in the non-eligible group ($p<0.001$).

Table 7.2 - Characteristics of the population eligible and non-eligible for the cycle of care

	Eligible % (95% CI) (n=403)	Non-eligible % (95% CI) (n=206)	P value
Female	47.2 (42.4-51.9)	30.8 (24.8-37.5)	<0.001
Age			
50-64	31.4 (27.0-36.2)	69.7 (63.2-75.6)	
65-74	34.2 (29.8-39.0)	26.2 (20.8-32.4)	
75+	34.2 (29.5-39.2)	4.1 (2.0-8.1)	<0.001
Self-reported health			
Excellent/very good	31.9 (27.5-36.7)	34.7 (28.4-41.6)	
Good	29.5 (25.1-34.3)	36.6 (30.3-43.4)	
Fair/poor	38.6 (33.8-43.6)	28.7 (22.5-35.7)	0.06
Education			
None/primary	60.4 (55.4-65.2)	28.3 (22.1-35.4)	
Secondary	32.2 (27.7-37.1)	46.4 (39.7-53.2)	
Third level	7.4 (5.6-9.7)	25.3 (20.1-31.4)	<0.001
Diabetes Management			
Insulin	17.4 (14.0-21.5)	9.9 (6.3-15.0)	<0.001
Tablets only	67.9 (63.0-72.4)	62.8 (55.9-69.2)	
No medication	14.7 (11.6-18.5)	27.4 (21.6-34.0)	
Diabetes-related condition			
Macro vascular	17.4 (14.0-21.4)	13.4 (9.1-19.3)	0.21
Micro vascular	28.1 (23.7-33.1)	22.7 (17.2-29.2)	0.16
GP			
Attended past year	98.1 (96.3-99.0)	91.8 (86.8-95.0)	<0.001
Mean (SD) no. visits past year	6.7 (5.2)	3.8 (3.9)	<0.001
OPD			
Attended past year	62.1 (57.0-66.9)	57.9 (50.3-65.1)	0.35
Mean (SD) no. visits past year	2.4 (2.8)	1.6 (2.4)	0.001
Hospital admissions			
Admitted in past year	22.4 (18.4-26.9)	14.6 (10.4-20.2)	0.03
Mean (SD) no. admissions past year	0.4 (0.8)	0.2 (0.6)	0.01
AE admissions			
Admitted in past year	21.9 (18.0-26.5)	17.9 (13.2-23.6)	0.23
Mean (SD) no. admissions past year	0.3 (0.8)	0.3 (0.8)	0.44
Access to ancillary state service	12.3 (9.2-16.2)	9.5 (5.9-15.0)	0.35
Dietician	19.8 (15.9-24.4)	6.8 (4.0-11.2)	<0.001
Chiropody services	27.0 (22.7-31.7)	7.0 (4.1-11.7)	<0.001
Optician	15.8 (12.4-19.9)	2.7 (1.2-6.0)	<0.001
Public health/community nurse	1.0 (0.4-2.3)	1.6 (0.5-5.3)	0.47
Psychology/counselling services			

7.5 Discussion

This study describes the proportion, demographics, health status and healthcare utilisation of people with type 2 diabetes according to their eligibility for the cycle of care initiative. Almost one third of people over the age of 50 years are not eligible for the initiative. They are more likely to be male, to be younger and to have higher levels of educational attainment than those covered by the scheme. There were no significant differences in self-reported health. However, there were significant differences in diabetes management and health service use.

The aim of the cycle of care is to provide financial remuneration to GPs for providing structured care for people with type 2 diabetes in primary care. National guidelines for integrated care identify those with uncomplicated type 2 diabetes as the most suitable to be managed in primary care (22). Our findings indicate that those currently not eligible for the scheme are more likely to fit the outlined criteria of uncomplicated diabetes and therefore suitable for structured care in a primary care setting. The prevalence of diabetes-related complications in the non-eligible population was lower than the eligible population, although this was not statistically significant. We find that almost double the proportion of the non-eligible population manage their diabetes without medication. Furthermore, a significantly lower proportion of the non-eligible population were on insulin. As it currently stands, the cycle of care eligibility is not based on clinical need but is solely means-tested. Integrated diabetes care has been shown to reduce preventable hospitalisations for diabetes-related complications (128). Structured approaches to diabetes care demonstrate improvements in glycaemic control and cardiovascular risk factors (129,130). However, if integrated diabetes care is to result in clinically and cost-effective care, it must be provided in the most appropriate setting to all people with diabetes (148).

In Ireland, attendance at out-patient clinics is free at the point of access creating a perverse incentive for non-eligible individuals to seek routine diabetes care in secondary care. The roll out of the cycle of care to all people with type 2 diabetes would remove the financial barriers that currently exist to managing uncomplicated diabetes at the right time and in the right place. For integrated care to be implemented, the financing has to be aligned with the care pathways.

Using a nationally representative sample, we provide robust estimates of the number of people aged 50 years and older who are currently not eligible for the cycle of care scheme. There are some limitations to be noted. Our estimates only include people aged over 50 years and so the total number of non-eligible people is likely to much higher. Self-reported doctor diagnoses may introduce misclassification bias and result in inaccurate estimates. However, a number of studies have demonstrated that self-report is a suitable method to determine the prevalence of diabetes compared to medical records (150,232). The self-reported doctor diagnosis of diabetes may underestimate the true prevalence of diabetes as it does not measure undiagnosed diabetes. However, the prevalence of undiagnosed diabetes has been shown to be low in this cohort (149). As TILDA does not contain information on diabetes specific health service, we were unable to explore attendance rates at outpatient departments compared to GP visits for routine diabetes care.

Our findings highlight the inequity of the cycle of care scheme, particularly for younger people with type 2 diabetes. While a welcome initiative and an important step in the implementation of integrated care in Ireland, eligibility for the scheme needs to be based on clinical criteria rather than income-based in order for the true benefits to be realised. If integrated diabetes care is to result in cost-effective care, it is essential that all those likely to benefit from the scheme are eligible.

8. Unmet Need for Bariatric Surgery

8.1 Abstract

Introduction

With the rising prevalence of severe obesity and type 2 diabetes, bariatric surgery offers a clinical and cost-effective treatment for carefully selected patients. Despite this, provision of surgical services varies significantly between countries. We aim to inform health service planning by estimating the number of people who would potentially benefit from bariatric surgery.

Methods

We applied two separate evidence-based criteria sets for eligibility for bariatric surgery. For the first set of criteria, we considered those with body mass index (BMI) ≥40kg/m² or ≥35kg/m² and one or more of the following; type 2 diabetes, hypertension, previous myocardial infarction (MI) or sleep apnea. For the second set of criteria, we considered patients with type 2 diabetes and BMI ≥35kg/m², with one or more of the following; previous MI, elevated urine albumin-creatinine ratio, retinopathy, neuropathy or peripheral vascular disease. Prevalence estimates were applied to census figures for 2011, estimating absolute numbers meeting the criteria.

Results

Among adults aged ≥50 years, 7.97% (95% CI: 7.23-8.78), representing 92,573 (95% CI: 83,978–101,981) people, met criteria one and 0.97% (95% CI :0.73-1.28), representing 11,231 (95% CI: 8,471–14,890) people, met criteria two. With fewer than 1/100,000

population publicly funded surgeries taking place annually, current service provision meets much less than 0.1% of the need.

Conclusion

While many adults who fulfil the eligibility criteria for bariatric surgery may not want or require it, the current level of need for bariatric surgical services is not being met. A strategy to develop and expand the provision of bariatric care is urgently needed.

8.2 Introduction

With the prevalence of severe obesity and type 2 diabetes continuing to rise (4,233–235), the increasing evidence on the clinical and cost-effectiveness of bariatric surgery makes it an attractive treatment option (236,237). A Cochrane review investigating the effect of bariatric surgery for overweight and obesity found surgery to be more clinically effective in the treatment of severe obesity than other non-surgical interventions (238). While most trials only follow participants for up to three years (132), data from observational studies with 10-20 year follow-up show the benefits of surgery (131,238). The Swedish Obese Subjects prospective case-control study, indicates the benefits of bariatric surgery in maintaining weight loss for 20 years (239). Compared with usual care, bariatric surgery is associated with a long-term reduction in overall morbidity and mortality (239,240). The largest benefit of bariatric surgery is observed among people with type 2 diabetes (240), with international diabetes organisations now calling for the inclusion of metabolic surgery among anti-diabetes interventions for people with type 2 diabetes and obesity (237). Substantially higher diabetes remission rates are observed among people with type 2 diabetes after bariatric surgery (adjusted odds ratios for remission after two years was 8.42; $P<0.001$ and 3.45; $P<0.001$ after ten years) (239) . In the UK national registry of bariatric surgical patients with diabetes, operated on between 2011 and 2013, 65% achieved good glycemic control, returning to a state of no indication of diabetes without medication (241). This represents a large reduction in direct healthcare cost associated with diabetes. The cost-effectiveness of bariatric surgery is most notable in patients with high direct health care costs secondary to the complications of obesity such as diabetes (131). A UK health technology assessment found for patients with diabetes and a body mass index (BMI) of 30-39kg/m^2 the incremental-cost-effective-ratio was £1367 per QALY gained (242). For patients with type 2 diabetes (ranging from newly diagnosed to those requiring multimodal therapies), the costs of surgery will be recuperated within three years (239,243). This can potentially be further improved in the subgroup of patients with type 2 diabetes with the highest direct healthcare costs, such as those requiring expensive insulin or GLP-1 analogues or the subgroup of patients with established complications of diabetes such as micro and macrovascular disease (244).

Despite the global obesity and diabetes epidemics and the demonstrated clinical and cost-effectiveness of bariatric surgery, there is large variation in service provision between countries. The rate of bariatric surgery in North America is 44 per 100,000 population, while Sweden performs 78 surgeries per 100,000 population. In comparison, the rate of surgery is <10 per 100,000 in the UK or Germany (245). Periodic assessment of bariatric surgery rates is an important source of knowledge to healthcare providers and governments (246). Further to this, in order to inform health policy and resource allocation, an estimate of the prevalence of eligibility for bariatric surgery would be helpful. Bariatric surgical procedures are not commonly performed in Ireland. There is currently no national registry of bariatric surgical patients, so robust information about how many procedures are done is limited. However, only two public bariatric centres exist nationally and between them fewer than 50 procedures are done per annum, equivalent to fewer than 1/100,000 population publicly funded surgeries taking place annually. Ireland has a two tier health system, whereby all citizens are entitled to health care under the public system, funded mainly through general taxation. Private health insurance acts as duplicate cover, providing faster access to care (247). While an unknown number of bariatric surgeries are carried out in the private sector, this provision is dependent on individuals' ability to pay.

Ireland has one of the highest rates of obesity in Europe, with one in four adults estimated to already suffer with obesity (247). The prevalence of doctor-diagnosed diabetes has increased from 2.2% of the adult population in 1998 to 5.2% in 2015 (47). The overall prevalence of type 2 diabetes among adults aged over 50 years in Ireland is 8.5% (47). We sought to estimate the number of people potentially eligible for bariatric surgery in Ireland based on established clinical criteria and then to refine the number of potentially eligible patients by identifying those who suffer from the diseases with high morbidity, mortality and healthcare cost, that respond best to bariatric surgery.

8.3 Methods

We applied two separate sets of criteria to identify those potentially eligible for bariatric surgery. The first set of criteria, based on UK guidelines (131), included a BMI ≥40 kg/m^2 or a BMI ≥35kg/m^2 and one or more of the following conditions; type 2 diabetes, hypertension, previous myocardial infarction (MI) and sleep apnea. The second set of criteria applied only to those patients with type 2 diabetes and BMI ≥35kg/m^2, who had one or more of the following; previous MI, elevated urine albumin-creatinine ratio, retinopathy, neuropathy or peripheral vascular disease. This second set of criteria was used to identify the cohort of patients in whom the largest benefits and cost-savings from bariatric surgery are observed (242,244).

We conducted a cross sectional analysis of the first wave (2009-2011) of The Irish LongituDinal Study on Ageing (TILDA) to estimate the proportion of people eligible for bariatric surgery. TILDA is a nationally representative cohort study of community-dwelling adults aged 50 years and over. The sampling frame is the Irish Geodirectory, which is a comprehensive and up-to-date list of all residential addresses in Ireland. A multistage probability sampling design was used, with each residential address in the country having an equal probability of selection. All household residents aged ≥50 years were eligible to participate in the study. Participants completed a computer-assisted personal interview

(CAPI) administered by trained social interviewers which included questions on self-report doctor diagnosis of chronic conditions. Those who completed the CAPI were invited to attend a health assessment either at the study centre or in their home (231). During the health assessment, trained nurses objectively measured participants' weight and height. These measures were used to calculate BMI. Only those who completed the health assessment are included in the analysis.

Individuals were classified as having diabetes if they self-reported a previous doctor diagnosis. Type 1 diabetes was defined as those who were aged less than 50 years at diabetes diagnosis and reported injecting insulin, but not taking oral hypoglycemic agents. All others were classified as having type 2 diabetes. Participants were asked "Has a doctor ever told you that you have any of the conditions on this card?", which included high blood pressure and heart attack (including MI or coronary thrombosis). Those who responded "yes" were considered to have the named condition. Participants were asked "How likely are you to doze off or fall asleep during the day?" with four different response options; 0=would never doze; 1=slight chance of dozing; 2=moderate chance of dozing; and 3=high chance of dozing. This question was considered a surrogate for the Epworth Sleepiness Scale (248). For the purpose of this analysis, those who responded with "high chance of dozing" were classified as having sleep apnea. Participants who reported a doctor diagnosis of diabetes during the CAPI were asked the question 'Has a doctor ever told you that you have any of the following conditions related to your diabetes?'. The conditions listed were: leg ulcer, protein in urine, lack of feeling and tingling pain in legs and feet due to nerve damage, damage to the back of your eye. Those who responded "yes" were considered to have peripheral vascular disease, elevated urine albumin-creatinine ratio, diabetic neuropathy or diabetic retinopathy, respectively.

Survey weights were applied to the analysis to reflect the complex sampling design and to adjust for participation bias. Based on comparisons with the Irish census and the 2010 Quarterly National Household Survey, a weight was constructed adjusting for differences in educational attainment, age, sex, marital status and geographic location. The survey weights applied also accounted for non-response bias in the health assessment sample, as previously described (134). The number of participants meeting the eligibility criteria for the two sets of criteria were calculated and expressed as a percentage with corresponding 95% confidence intervals, using Poisson regression. Prevalence estimates were applied to the most recent Irish census figures (2011) to determine absolute numbers meeting these criteria. Based on evidence from the UK national registry of bariatric surgical patients, a diabetes remission rate of 65% was applied to model the number of people with type 2 diabetes and microvascular complications (criteria 2) with potential remission of diabetes following surgery (241). Due to the crude measure used for sleep apnea, a sensitivity analysis was conducted excluding those who were defined as eligible for surgery based solely on having sleep apnea. Analysis was carried out in Stata v.12 for windows (StataCorp, College Station, TX, USA) using the survey function (svy).

8.4 Results

A total of 8,175 participants from 6,282 households completed the CAPI (response rate: 62%). Of these, 5,873 (71%) participants completed the health assessment and were included in the analysis. The cohort comprised of 51.7% females and the mean age was 62.9 years. 21.2% (95% CI: 20.1, 2.4) had a normal BMI and 42.7% (95% CI: 41.4, 44.1) had a BMI between 25kg/m^2 and 29.9kg/m^2. 25.2% (95% CI: 24.1, 26.4) of the population had moderate obesity while 7.7% (95% CI: 7.0, 8.5) and 2.7% (95% CI: 2.3, 3.1) had severe and morbid obesity, respectively. The prevalence of type 2 diabetes was 7.74% (95% CI: 7.08, 8.45) and the prevalence of doctor-diagnosed hypertension was 37.9% (95% CI: 36.5, 39.3).

Under criteria one, 444 participants were eligible for bariatric surgery (patients with a BMI ≥40 or ≥35kg/m² and one or more of the following conditions; type 2 diabetes, hypertension, previous MI or sleep apnea). This accounted for 7.97% (95% CI: 7.23, 8.78) of the population (**Table 8.1**). In the sensitivity analysis excluding those eligible for surgery based solely on having sleep apnea, this reduced to 7.42% (95% CI: 6.72, 8.19).

Table 8.1 - Distribution of clinical conditions among TILDA participants for criteria one

Condition	N	% (95% CI)	Population Estimates N (95% CI)
BMI ≥40kg/m²	145	2.66 (2.25, 3.13)	
BMI ≥35kg/m² and:			
Type 2 diabetes	112	2.06 (1.70, 2.49)	
Hypertension	336	6.08 (5.43, 6.79)	
Previous MI	37	0.67 (0.48, 0.94)	
Sleep apnea	119	2.19 (1.81, 2.65)	
Any	444	7.97 (7.23, 8.78) [a]	92,573 (83,978 – 101,981)

[a]Categories of participants are not mutually exclusive
TILDA – The Irish LongituDinal study of Aging
BMI – Body mass index
MI – Myocardial infarction

There were 112 (2.06% [95% CI: 1.70, 2.49) participants with a BMI ≥35kg/m² and type 2 diabetes. Under the second set of criteria, 50 participants were eligible for bariatric surgery (patients with a BMI ≥35kg/m², type 2 diabetes and one or more of the following complications; previous MI, elevated urine albumin creatinine ratio, retinopathy, neuropathy, and peripheral vascular disease). This accounted for 0.97% (95% CI: 0.73, 1.28) of the population (**Table 8.2**).

Table 8.2 - Distribution of complications among TILDA participants with BMI ≥35kg/m² and type 2 diabetes (criteria two)

Condition	N	% (95% CI)	Population Estimates N (95% CI)
Previous MI	15	0.29 (0.17, 0.50)	
Protein in urine	14	0.25 (0.15, 0.41)	
Retinopathy	17	0.36 (0.22, 0.58)	
Neuropathy	21	0.39 (0.25, 0.60)	
Peripheral vascular disease	10	0.19 (0.10, 0.35)	
Any	50	0.97 (0.73, 1.28)[a]	11,231 (95% CI: 8,471, 14,890)

[a]Categories of participants are not mutually exclusive
TILDA – The Irish LongituDinal study of Aging
BMI – Body mass index
MI – Myocardial infarction

The total proportion of people eligible for bariatric surgery under the two sets of criteria were applied to the 2011 Irish census figures to estimate the absolute numbers with potential indication for bariatric surgery in Ireland. The total population aged ≥50 years was 1,161,512. The total number of people with potential indication for bariatric surgery under the first set of criteria, was 92,573 (95% CI: 83,978, 101,981). Under the second set of criteria, 11,231 (95% CI: 8,471, 14,890) people were eligible for bariatric surgery.

The UK national registry of patients with diabetes operated on between 2011 and 2013, shows 65% had acceptable glycaemic control without medication after surgery (241). By applying these results to Irish patients with complicated type 2 diabetes (criteria 2), we estimated that prioritising bariatric surgery for this cohort could result in an estimated 7,301 patients achieving good glycaemic control, without requiring medication for up to two years after surgery.

8.5 Discussion

It is evident that a substantial proportion of older Irish adults are potentially eligible for bariatric surgery. While many adults who fulfil the criteria may not want or be suitable for bariatric surgery, these findings highlight the high level of need for such services in Ireland. With an estimated 1/100,000 population publically funded surgeries taking place annually, our findings indicate that current public service provision of bariatric surgery in Ireland meets much less than 0.1% of the need. This mirrors the situation in other countries, such as the UK where it is estimated that 2.5 million people are eligible for surgery with less than 10,000 surgeries occurring annually (131).

Obesity poses a major challenge for public health. Public health strategies focus on the prevention of obesity and lifestyle interventions. However, it is clear that the treatment of morbid obesity needs to be recognised as a fundamental aspect in tackling the obesity epidemic. A strategy to develop bariatric care in Ireland seems warranted, given the previously established efficacy and cost-effectiveness of bariatric surgery. This effective intervention increases life-expectancy and increases the odds of diabetes remission, leading to a reduction in direct healthcare expenditure (131). The challenge will be to implement a strategy that can show a return on investment within three years, but which will have an acceptable budget impact in the first year (243). This may be achieved by focusing on those patients that would benefit most from surgery while simultaneously having the highest direct healthcare cost such as those with established complications of diabetes (criteria two) who are using expensive drugs to treat their diabetes. Our findings demonstrate that by increasing the rates of surgery in Ireland in line with other European countries, such as France (57/100,000), the intervention will be more accessible, at least, to this population subgroup (245).

A strength of this study is the large national population based sample. The objective measurement of BMI reduces the potential for misclassification bias. The data are weighted to adjust for differential non-response, minimising the potential for selection bias and improving the representativeness of the findings. A number of limitations should be noted. Firstly, the reliance on self-reported doctor diagnoses may introduce misclassification bias and result in inaccurate estimates. However, a number of studies have demonstrated that self-report is a suitable method to determine the prevalence of type 2 diabetes, hypertension and previous MI compared to medical records (150,232). The self-reported doctor diagnosis of diabetes may underestimate the true prevalence of type 2 diabetes as it does not measure undiagnosed diabetes. However, the prevalence of undiagnosed diabetes is low in this cohort (149). Moreover, such an underestimation in the prevalence of diabetes would likely lead to an underestimation of the true prevalence of eligibility for bariatric surgery also. As there was no validated measure for sleep apnoea in TILDA, our assessment of its prevalence is relatively crude and may have lacked adequate specificity. However, sleep apnoea prevalence, using this measure, was similar to prevalence estimates in other cohorts of older adults (249,250). Moreover, a sensitivity analysis, whereby sleep apnoea was omitted from the eligibility criteria, showed no significant difference in the prevalence of eligibility for surgery. Thus, our estimates of the prevalence of bariatric surgical eligibility are likely to be conservative and clearly limited to those aged 50 years and older. The true numbers eligible for bariatric surgery in Ireland are likely to be higher.

In conclusion, 7.97% of older Irish adults are eligible for bariatric surgery according to recent guidelines but current service provision meets less than 0.1% of this need. This huge gap between need and service highlights the urgent need for the provision of clinical and cost-effective interventions to treat people with severe obesity. Our findings ought to be considered by policy makers and should be used to guide resource allocation. One strategy to limit the budget impact is to focus on the 0.97% of patients, eligible under criteria two, that have very large and immediate impacts on their health and healthcare cost. The provision of bariatric surgery to those in greatest need has the potential to improve both patient outcomes and reduce direct healthcare expenditure quickly.

O'Neill, K. N. 2018. The economic burden of diabetes in Ireland. PhD Thesis, University College Cork.

Please note that Chapter 9 (pp. 136-151) is unavailable due to a restriction requested by the author.

10. References

1. Zimmet PZ, Magliano DJ, Herman WH, Shaw JE. Diabetes: A 21st century challenge. Lancet Diabetes Endocrinol [Internet]. 2014;2(1):56–64. Available from: http://dx.doi.org/10.1016/S2213-8587(13)70112-8

2. Vos T, Barber RM, Bell B, Bertozzi-Villa A, Biryukov S, Bolliger I, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015;386(9995):743–800.

3. Naghavi M, Abajobir AA, Abbafati C, Abbas KM, Abd-Allah F, Abera SF, et al. Global, regional, and national age-sex specifc mortality for 264 causes of death, 1980-2016: A systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390(10100):1151–210.

4. NCD Risk Factor Collaboration. Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4·4 million participants. Lancet [Internet]. 2016;387(10027):1513–30. Available from: http://dx.doi.org/10.1016/S0140-6736(16)00618-8

5. Bommer C, Heesemann E, Sagalova V, Manne-Goehler J, Atun R, Bärnighausen T, et al. The global economic burden of diabetes in adults aged 20–79 years: a cost-of-illness study. Lancet Diabetes Endocrinol [Internet]. 2017;3633:423–30. Available from: http://linkinghub.elsevier.com/retrieve/pii/S2213858717300979

6. Zhang P, Zhang X, Brown J, Vistisen D, Sicree R, Shaw J, et al. Global healthcare expenditure on diabetes for 2010 and 2030. Diabetes Res Clin Pract [Internet]. 2010;87(3):293–301. Available from: http://dx.doi.org/10.1016/j.diabres.2010.01.026

7. Bommer C, Sagalova V, Heesemann E, Manne-goehler J, Atun R. Global Economic Burden of Diabetes in Adults : Projections From 2015 to 2030. Diabetes Care. 2018;41(May):1–8.

8. American Diabetes Association. Economic Costs of Diabetes in the U.S. in 2017. Diabetes Care [Internet]. 2018;41(May):dci180007. Available from: http://care.diabetesjournals.org/lookup/doi/10.2337/dci18-0007

9. Zhuo X, Zhang P, Kahn HS, Bardenheier BH, Li R, Gregg EW. Change in medical spending attributable to diabetes: National data from 1987 to 2011. Diabetes Care. 2015;38(4):581–7.

10. Zhang P, Gregg E. Global economic burden of diabetes and its implications. Lancet Diabetes Endocrinol [Internet]. 2017;5(6):404–5. Available from: http://linkinghub.elsevier.com/retrieve/pii/S2213858717301006

11. Seuring T, Archangelidi O, Suhrcke M, Seuring T, Suhrcke ÁM, Archangelidi O, et al. The Economic Costs of Type 2 Diabetes: A Global Systematic Review. Pharmacoeconomics. 2015;33:811–31.

12. Venkat Narayan KM. Type 2 diabetes: Why we are winning the battle but losing the war? 2015 Kelly west award lecture. Diabetes Care. 2016;39(5):653–63.

13. Gregg EW, Albright AL. The public health response to diabetes--two steps forward, one step back. JAMA. 2009;301(15):1596–8.

14. McKinlay J, Marceau L. US public health and the 21st century: diabetes mellitus. Lancet [Internet]. 2000;356(9231):757–61. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0140673600026416

15. Glasgow RE, Wagner EH, Kaplan RM, Vinicor F, Smith L, Norman J. If diabetes is a public health problem, why not treat it as one? A population-based approach to chronic illness. Ann Behav Med [Internet]. 1999 Jun 1;21(2):159–70. Available from: http://dx.doi.org/10.1007/BF02908297

16. White M. Population Approaches to Prevention of Type 2 Diabetes. PLoS Med. 2016;13(7):10–3.

17. Roberts S, Barry E, Craig D, Airoldi M, Bevan G, Greenhalgh T. Preventing type 2 diabetes: systematic review of studies of cost-effectiveness of lifestyle programmes and metformin, with and without screening, for pre-diabetes. BMJ Open. 2017;7(11):e017184.

18. Vinicor F. Is diabetes a public-health disorder? Diabetes Care. 1994;17(Suppl 1):22–7.

19. The Lancet Public Health. Obesity: the sweet revenge of tax. The Lancet Public Health [Internet]. 2017;2. Available from: http://dx.doi.org/10.1016/S2468-2667(16)30041-X

20. Departement of Finance. Sugar-Sweetened Drinks Tax - Budget 2018 - Information Note [Internet]. 2017. Available from: http://www.budget.gov.ie/Budgets/2018/Documents/Sugar Sweetened Drinks Tax.pdf

21. Cornelsen L, Carreido A. Health related taxes on foods and beverages. Food Res Collab Brief Pap. 2015;1–23.

22. Harkins V. A Practical Guide to Integrated Type 2 Diabetes Care. [Internet]. 2016. Available from: https://www.hse.ie/eng/services/list/2/primarycare/east-coast-diabetes-service/management-of-type-2-diabetes/diabetes-and-pregnancy/icgp-guide-to-integrated-type-2.pdf

23. Department of Health. A Healthy Weight for Ireland - Obesity Policy and Action Plan 2016-2025. 2016.

24. Majumdar SR, Soumerai SB. The unhealthy state of health policy research. Health Aff. 2009;28(5):900–8.

25. Fradkin J, Roberts B, Rodgers G. What's Preventing Us from Preventing Type 2 Diabetes? N Engl J Med [Internet]. 2012;367(13):1177–9. Available from: http://scholar.google.com/scholar?hl=en&btnG=Search&q=intitle:New+engla+nd+journal#0

26. Rice DP. Cost of illness studies: what is good about them? Inj Prev. 2000;6:177–80.

27. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2009;32(SUPPL. 1).

28. Holman N, Young B, Gadsby R. Current prevalence of Type 1 and Type 2 diabetes in adults and children in the UK. Diabet Med [Internet]. 32(9):1119–20. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/dme.12791

29. Xu G, Liu B, Sun Y, Du Y, Snetselaar LG, Hu FB, et al. Prevalence of diagnosed type 1 and type 2 diabetes among US adults in 2016 and 2017: population based study. BMJ [Internet]. 2018;361:k1497. Available from: http://www.bmj.com/lookup/doi/10.1136/bmj.k1497%0Ahttps://www.bmj.com/content/362/bmj.k1497

30. DiMeglio LA, Evans-Molina C, Oram RA. Type 1 diabetes. Lancet [Internet]. 2018;391(10138):2449–62. Available from: http://dx.doi.org/10.1016/S0140-6736(18)31320-5

31. Zimmet P, Alberti KGMM, Shaw J. Global and Societal Implications of the Diabetes Epidemic. Nature [Internet]. 2001;414(December 2001):782–787. Available from: http://www.nature.com/nature/journal/v414/n6865/pdf/414782a.pdf

32. Gregg EW, Sattar N, Ali MK. The changing face of diabetes complications. Lancet Diabetes Endocrinol [Internet]. 2016;4(6):537–47. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27156051

33. Gerstein HC, Werstuck GH. Dysglycaemia, vasculopenia, and the chronic consequences of diabetes. Lancet Diabetes Endocrinol. 2013;1(1):71–8.

34. Lu FP, Lin KP, Kuo HK. Diabetes and the risk of multi-system aging phenotypes: A systematic review and meta-analysis. PLoS One. 2009;4(1).

35. Giovannucci E, Harlan DM, Archer MC, Bergenstal RM. Diabetes and Cancer : A Consensus Report. CA Cancer J Clin. 2010;60(4):207–21.

36. Vigneri P, Frasca F, Sciacca L, Pandini G, Vigneri R. Diabetes and cancer. Endocr Relat Cancer. 2009;16(4):1103–23.

37. Wild S, Roglic G, Green A, Sicree R, Hilary K. Global Prevalence of Diabetes: Estimates for the year 2000 and projection for 2030. Diabetes Care. 2004;27(5):1047–53.

38. Cheng YJ, Imperatore G, Geiss LS, Wang J, Saydah SH, Cowie CC, et al. Secular changes in the age-specific prevalence of diabetes among U.S. adults: 1988-2010. Diabetes Care. 2013;36(9):2690–6.

39. Ogurtsova K, da Rocha Fernandes JD, Huang Y, Linnenkamp U, Guariguata L, Cho NH, et al. IDF Diabetes Atlas: Global estimates for the prevalence of diabetes for 2015 and 2040. Diabetes Res Clin Pract [Internet]. 2017;128:40–50. Available from: http://dx.doi.org/10.1016/j.diabres.2017.03.024

40. Cho NH, Shaw JE, Karuranga S, Huang Y, da Rocha Fernandes JD, Ohlrogge AW, et al. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract [Internet]. 2018;138:271–81. Available from: https://doi.org/10.1016/j.diabres.2018.02.023

41. LS G, Wang J, YJ C, al et. Prevalence and incidence trends for diagnosed diabetes among adults aged 20 to 79 years, united states, 1980-2012. JAMA [Internet]. 2014 Sep 24;312(12):1218–26. Available from: http://dx.doi.org/10.1001/jama.2014.11494

42. Sharma M, Nazareth I, Petersen I. Trends in incidence, prevalence and prescribing in type 2 diabetes mellitus between 2000 and 2013 in primary care: a retrospective cohort study. BMJ Open [Internet]. 2016;6(1):e010210. Available from:

http://bmjopen.bmj.com/content/6/1/e010210.abstract

43. Read SH, Kerssens JJ, McAllister DA, Colhoun HM, Fischbacher CM, Lindsay RS, et al. Trends in type 2 diabetes incidence and mortality in Scotland between 2004 and 2013. Diabetologia [Internet]. 2016;59(10):2106–13. Available from: http://dx.doi.org/10.1007/s00125-016-4054-9

44. Carstensen B, Kristensen JK, Ottosen P, Borch-Johnsen K. The Danish National Diabetes Register: Trends in incidence, prevalence and mortality. Diabetologia. 2008;51(12):2187–96.

45. Jansson SPO, Fall K, Brus O, Magnuson A, Wändell P, Östgren CJ, et al. Prevalence and incidence of diabetes mellitus: a nationwide population-based pharmaco-epidemiological study in Sweden. Diabet Med [Internet]. 32(10):1319–28. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/dme.12716

46. Tracey ML, Gilmartin M, O'Neill K, Fitzgerald A, McHugh S, Buckley C, et al. Epidemiology of diabetes and complications among adults in the Republic of Ireland 1998-2015: A systematic review and meta-analysis. BMC Public Health [Internet]. 2016;16(132). Available from: http://dx.doi.org/10.1186/s12889-016-2818-2

47. Tracey ML, Mchugh SM, Buckley CM, Canavan RJ, Fitzgerald AP, Kearney PM. The prevalence of Type 2 diabetes and related complications in a nationally representative sample of adults aged 50 and over in the Republic of Ireland. Diabet Med. 2016;33(4):441–5.

48. Sinnott S-J, McHugh S, Whelton H, Layte R, Barron S, Kearney PM. Estimating the prevalence and incidence of type 2 diabetes using population level pharmacy claims data: a cross-sectional study. BMJ Open Diabetes Res Care [Internet]. 2017;5(1):e000288. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28123753%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC5253438%5Cnhttp://drc.bmj.com/lookup/doi/10.1136/bmjdrc-2016-000288

49. Vos T, Abajobir AA, Abbafati C, Abbas KM, Abate KH, Abd-Allah F, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: A systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390(10100):1211–59.

50. van Dieren S, Beulens JWJ, van der Schouw YT, Grobbee DE, Neal B. The global burden of diabetes and its complications: an emerging pandemic. Eur J Cardiovasc Prev Rehabil. 2010 May;17 Suppl 1:S3-8.

51. Shah AD, Langenberg C, Rapsomaniki E, Denaxas S, Pujades-Rodriguez M, Gale CP, et al. Type 2 diabetes and incidence of cardiovascular diseases: A cohort study in 1·9 million people. Lancet Diabetes Endocrinol. 2015;3(2):105–14.

52. Buckley CM, O'Farrell A, Canavan RJ, Lynch AD, De La Harpe D V, Bradley CP, et al. Trends in the incidence of lower extremity amputations in people with and without diabetes over a five-year period in the Republic of Ireland. PLoS One [Internet]. 2012;7(7):e41492. Available from: http://www.scopus.com/inward/record.url?eid=2-s2.0-84864450275&partnerID=tZOtx3y1

53. Sarwar N, Gao P, Kondapally Seshasai SR, Gobin R, Kaptoge S, Di Angelantonio E, et

al. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: A collaborative meta-analysis of 102 prospective studies. Lancet [Internet]. 2010;375(9733):2215–22. Available from: http://dx.doi.org/10.1016/S0140-6736(10)60484-9

54. Gregg EW, Li Y, Wang J, Burrows NR, Ali MK, Rolka D, et al. Changes in diabetes-related complications in the United States, 1990-2010. N Engl J Med [Internet]. 2014;370(16):1514–23. Available from: http://www.nejm.org/doi/pdf/10.1056/NEJMoa1310799

55. Booth GL, Kapral MK, Fung K, Tu J V. Recent trends in cardiovascular complications among men and women with and without diabetes. Diabetes Care. 2006;29(1):32–7.

56. Pop-Busui R, Boulton AJM, Feldman EL, Bril V, Freeman R, Malik RA, et al. Diabetic neuropathy: A position statement by the American diabetes association. Diabetes Care. 2017;40(1):136–54.

57. Winell K, Venermo M, Ikonen T, Sund R. Indicators for comparing the incidence of diabetic amputations: A nationwide population-based register study. Eur J Vasc Endovasc Surg [Internet]. 2013;46(5):569–74. Available from: http://dx.doi.org/10.1016/j.ejvs.2013.07.010

58. Kurowski JR, Nedkoff L, Schoen DE, Knuiman M, Norman PE, Briffa TG. Temporal trends in initial and recurrent lower extremity amputations in people with and without diabetes in Western Australia from 2000 to 2010. Diabetes Res Clin Pract [Internet]. 2015;108(2):280–7. Available from: http://dx.doi.org/10.1016/j.diabres.2015.02.008

59. Lombardo FL, Maggini M, De Bellis A, Seghieri G, Anichini R. Lower extremity amputations in persons with and without diabetes in Italy: 2001-2010. PLoS One. 2014;9(1):1–7.

60. Van Houtum WH, Rauwerda JA, Ruwaard D, Schaper NC, Bakker K. Reduction in Diabetes-Related Lower-Extremity Amputations in the Netherlands: 1991-2000. Diabetes Care. 2004;27(5):1042–6.

61. Ikonen TS, Sund R, Venermo M, Winell K. Fewer major amputations among individuals with diabetes in Finland in 1997-2007: A population-based study. Diabetes Care. 2010;33(12):2598–603.

62. Kennon B, Leese GP, Cochrane L, Colhoun H, Wild S, Stang D, et al. Reduced incidence of lower-extremity amputations in people with diabetes in Scotland: A nationwide study. Diabetes Care. 2012;35(12):2588–90.

63. Klein BEK. Overview of Epidemiologic Studies of Diabetic Retinopathy. Ophthalmic Epidemiol [Internet]. 2007;14(4):179–83. Available from: https://doi.org/10.1080/09286580701396720

64. Bunce C, Xing W, Wormald R. Causes of blind and partial sight certifications in England and Wales: April 2007-March 2008. Eye [Internet]. 2010;24(11):1692–9. Available from: http://dx.doi.org/10.1038/eye.2010.122

65. Arora S, Kolb S, Goyder E, McKibbin M. Trends in the incidence of visual impairment certification secondary to diabetic retinopathy in the Leeds metropolitan area,

2005–2010. Diabet Med [Internet]. 29(7):e112–6. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1464-5491.2012.03619.x

66. Yau JWY, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, et al. Global Prevalence and Major Risk Factors of Diabetic Retinopathy. Diabetes Care [Internet]. 2012;35(3):556–64. Available from: http://care.diabetesjournals.org/cgi/doi/10.2337/dc11-1909

67. Skaat A, Chetrit A, Belkin M, Kinori M, Kalter-Leibovici O. Time Trends in the Incidence and Causes of Blindness in Israel. Am J Ophthalmol [Internet]. 2012 Feb 1;153(2):214-221.e1. Available from: https://doi.org/10.1016/j.ajo.2011.08.035

68. Genz J, Scheer M, Trautner C, Zöllner I, Giani G, Icks A. Reduced incidence of blindness in relation to diabetes mellitus in southern Germany? Diabet Med [Internet]. 27(10):1138–43. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1464-5491.2010.03081.x

69. Tracey ML, Mchugh SM, Fitzgerald AP, Buckley CM, Canavan RJ, Kearney PM. Trends in blindness due to diabetic retinopathy among adults aged 18 – 69 years over a decade in Ireland. Diabetes Res Clin Pract [Internet]. 2016;121:1–8. Available from: http://dx.doi.org/10.1016/j.diabres.2016.08.016

70. McHugh S, Tracey MLL, Riordan F, O'Neill K, Mays N, Kearney PMM, et al. Evaluating the implementation of a national clinical programme for diabetes to standardise and improve services: a realist evaluation protocol. Implement Sci [Internet]. 2015;11(1):107. Available from: http://implementationscience.biomedcentral.com/articles/10.1186/s13012-016-0464-9

71. Bardenheier BH, Lin J, Zhuo X, Ali MK, Thompson TJ, Cheng YJ, et al. Disability-free life-years lost among adults aged ≥50 years with and without diabetes. Diabetes Care. 2016;39(7):1222–9.

72. Cappuccio FP, Danaei G, Lu Y, Singh GM, Carnahan E, Stevens GA, et al. Cardiovascular disease, chronic kidney disease, and diabetes mortality burden of cardiometabolic risk factors from 1980 to 2010: A comparative risk assessment. Lancet Diabetes Endocrinol [Internet]. 2014;2(8):634–47. Available from: http://dx.doi.org/10.1016/S2213-8587(14)70102-0

73. Roper NA, Bilous RW, Kelly WF, Unwin NC, Connolly VM. Cause-specific mortality in a population with diabetes: South tees diabetes mortality study. Diabetes Care. 2002;25(1):43–8.

74. Haffner S, Letho S, Ronnemaa T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjecst with and without prior myocardial infarction. N Engl J Med. 1998;339(4):229–34.

75. Laing SP, Swerdlow AJ, Slater SD, Burden AC, Morris A, Waugh NR, et al. Mortality from heart disease in a cohort of 23,000 patients with insulin-treated diabetes. Diabetologia. 2003;46(6):760–5.

76. Tancredi M, Rosengren A, Svensson A-M, Kosiborod M, Pivodic A, Gudbjörnsdottir S, et al. Excess Mortality among Persons with Type 2 Diabetes. N Engl J Med [Internet]. 2015;373(18):1720–32. Available from: http://www.nejm.org/doi/10.1056/NEJMoa1504347

77. IDF Diabetes Altas Group. Update of mortality attributable to diabetes for the IDF Diabetes Atlas: Estimates for the year 2013. Diabetes Res Clin Pract [Internet]. 2015;109(3):461–5. Available from: http://dx.doi.org/10.1016/j.diabres.2015.05.037

78. Emerging Risk Factors Collaboration. Diabetes Mellitus, Fasting Glucose, and Risk of Cause-Specific Death. N Engl J Med. 2014;364(9):829–41.

79. Gregg EW, Cheng YJ, Saydah S, Cowie C, Garfield S, Geiss L, et al. Trends in Death Rates Among U.S. Adults With and Without Diabetes Between 1997 and 2006: Findings from the National Health Interview Survey. Diabetes Care [Internet]. 2012;35(6):1252–7. Available from: http://care.diabetesjournals.org/cgi/doi/10.2337/dc11-1162

80. Lind M, Garcia-Rodriguez LA, Booth GL, Cea-Soriano L, Shah BR, Ekeroth G, et al. Mortality trends in patients with and without diabetes in Ontario, Canada and the UK from 1996 to 2009: A population-based study. Diabetologia. 2013;56(12):2601–8.

81. Harding JL, Shaw JE, Peeters A, Guiver T, Davidson S, Magliano DJ. Mortality Trends Among People With Type 1 and Type 2 Diabetes in Australia: 1997–2010. Diabetes Care [Internet]. 2014;37(9):2579–86. Available from: http://care.diabetesjournals.org/lookup/doi/10.2337/dc14-0096

82. Gregg EW, Zhuo X, Cheng YJ, Albright AL, Venkat Narayan KM, Thompson TJ. Trends in lifetime risk and years of life lost due to diabetes in the USA, 1985–2011: a modelling study. Lancet Diabetes Endocrinol. 2014;2(11):867–74.

83. Narayan K, Boyle J, Thompson T, Sorensen S, Williamson D. Lifetime risk for diabetes mellitus in the united states. JAMA [Internet]. 2003 Oct 8;290(14):1884–90. Available from: http://dx.doi.org/10.1001/jama.290.14.1884

84. Narayan K, Boyle JP, Geiss LS, Saaddine JB, Thompson TJ. Impact of recent increase in incidence on future diabetes burden: U.S., 2005-2050. Diabetes Care. 2006;29(9):2114–6.

85. Ettaro L, Songer T, Zhang P, Engelgau M. Cost-of-Illness Studies in Diabetes Mellitus. Pharmacoeconomics. 2004;22(3):149–64.

86. Ng CS, Lee JYC, Toh MPHS, Ko Y. Cost-of-illness studies of diabetes mellitus: A systematic review. Diabetes Res Clin Pract. 2014;105(2):151–63.

87. Herman WH. The economic costs of diabetes: Is it time for a new treatment paradigm? Diabetes Care. 2013;36(4):775–6.

88. Akobundu E, Ju J, Blatt L, Mullins D. Cost-of-illness studies: A review of current methods. Pharmacoeconomics. 2006;24(9):869–90.

89. Jo C. Cost-of-illness studies : concepts , scopes , and methods. Clin Mol Hepatol. 2014;20:327–37.

90. Byford S, Torgerson DJ, Raftery J. Cost of illness studies. BMJ. 2000;320:1335.

91. Jefferson T, Demicheli V, Mugford M. Elementary Economic Evaluation in Health Care. 2nd ed. London: BMJ Publishing Group; 2000.

92. Honeycutt AA, Segel JE, Hoerger TJ, Finkelstein EA. Comparing cost-of-illness estimates from alternative approaches: An application to diabetes. Health Serv Res.

2009;44(1):303–20.

93. Tunceli O, Wade R, Gu T, Bouchard JR, Aagren M, Luo W. Cost of diabetes: comparison of disease-attributable and matched cohort cost estimation methods. Curr Med Res Opin. 2010;26(8):1827–34.

94. Calderón-Larrañaga A, Abad-Díez JM, Gimeno-Feliu LA, Marta-Moreno J, González-Rubio F, Clerencia-Sierra M, et al. Global health care use by patients with type-2 diabetes: Does the type of comorbidity matter? Eur J Intern Med [Internet]. 2015;26(3):203–10. Available from: http://dx.doi.org/10.1016/j.ejim.2015.02.011

95. Yang W, Zhao W, Xiao J, Li R, Zhang P, Kissimova-Skarbek K, et al. Medical Care and Payment for Diabetes in China: Enormous Threat and Great Opportunity. PLoS One. 2012;7(9).

96. Nolan JJ, O'Halloran D, McKenna TJ, Firth R, Redmond S. The cost of treating type 2 diabetes (CODEIRE). Ir Med J. 2006;100(9):307–10.

97. Ozieh MN, Bishu KG, Dismuke CE, Egede LE. Trends in health care expenditure in U.S. adults with Diabetes: 2002-2011. Diabetes Care. 2015;38(10):1844–51.

98. Jönsson B. Revealing the cost of Type II diabetes in Europe. Diabetologia. 2002;45(7):S5-12.

99. Yang W, Dall TM, Halder P, Gallo P, Kowal SL, Hogan PF, et al. Economic costs of diabetes in the U.S. in 2012. Diabetes Care [Internet]. 2013;36(4):1033–46. Available from: http://care.diabetesjournals.org/cgi/doi/10.2337/dc12-2625

100. Bruno G, Picariello R, Petrelli A, Panero F, Costa G, Cavallo-Perin P, et al. Direct costs in diabetic and non diabetic people: The population-based Turin study, Italy. Nutr Metab Cardiovasc Dis [Internet]. 2012;22(8):684–90. Available from: http://dx.doi.org/10.1016/j.numecd.2011.04.007

101. Sabale U, Bodegård J, Sundström J, Östgren CJ, Nilsson P, Johansson G, et al. Healthcare utilization and costs following newly diagnosed type-2 diabetes in Sweden: A follow-up of 38,956 patients in a clinical practice setting. Prim Care Diabetes [Internet]. 2015;9(5):330–7. Available from: http://dx.doi.org/10.1016/j.pcd.2015.01.001

102. Oliva J, Lobo F, Molina B, Monereo S. Direct Health Care Costs of Diabetic Patients in Spain. Diabetes Care. 2004;27:216–2621.

103. Esteghamati A, Khalilzadeh O, Anvari M, Meysamie A, Abbasi M, Forouzanfar M, et al. The economic costs of diabetes: A population-based study in Tehran, Iran. Diabetologia. 2009;52(8):1520–7.

104. Köster I, Von Ferber L, Ihle P, Schubert I, Hauner H. The cost burden of diabetes mellitus: The evidence from Germany - The CoDiM study. Diabetologia. 2006;49(7):1498–504.

105. Chodick G, Heymann AD, Wood F, Kokia E. The direct medical cost of diabetes in Israel. Eur J Heal Econ. 2005;6(2):166–71.

106. Sortsø C, Green A, Jensen PB, Emneus M. Societal costs of diabetes mellitus in Denmark. Diabet Med. 2015;877–85.

107. Hex N, Bartlett C, Wright D, Taylor M, Varley D. Estimating the current and future

costs of Type 1 and Type 2 diabetes in the UK, including direct health costs and indirect societal and productivity costs. Diabet Med [Internet]. 2012;29(7):855–62. Available from: http://doi.wiley.com/10.1111/j.1464-5491.2012.03698.x

108. Pagano E, De Rosa M, Rossi E, Cinconze E, Marchesini G, Miccoli R, et al. The relative burden of diabetes complications on healthcare costs: the population-based ARNO Diabetes Observatory, Italy. Nutr Metab Cardiovasc Dis [Internet]. 2016;1–7. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0939475315303094

109. Leśniowska J, Schubert A, Wojna M, Skrzekowska-Baran I, Fedyna M. Costs of diabetes and its complications in Poland. Eur J Heal Econ. 2014;15(6):653–60.

110. Williams R, Gaal L Van, Lucioni C. Assessing the impact of complications on the costs of Type II diabetes. Diabetologia. 2002;45(7):S13–7.

111. Ohinmaa A, Jacobs P, Pharmd SS, Johnson JA. The projection of prevalence and cost of diabetes in Canada: 2000 to 2016. Can J Diabetes [Internet]. 2004;28(2):1–8. Available from: http://scholar.google.com/scholar?hl=en&btnG=Search&q=intitle:The+Projection+of+Prevalence+and+Cost+of+Diabetes+in+Canada:+2000+to+2016#0%5Cnhttp://scholar.google.com/scholar?hl=en&btnG=Search&q=intitle:The+projection+of+prevalence+and+cost+of+diabetes+in+C

112. Trogdon JG, Hylands T. Nationally representative medical costs of diabetes by time since diagnosis. Diabetes Care. 2008;31(12):2307–11.

113. Medicines in Development. Medicines in Development for Diabetes [Internet]. Washington; 2016. Available from: http://phrma-docs.phrma.org/files/dmfile/medicines-in-development-report-diabetes.pdf

114. Nathan DM. Diabetes Advances in Diagnosis and Treatment. Jama [Internet]. 2015;314(10):1052. Available from: http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.2015.9536

115. Qaseem A, Barry MJ, Humphrey LL, Forciea MA, Fitterman N, Boyd C, et al. Oral pharmacologic treatment of type 2 diabetes mellitus: A clinical practice guideline update from the American college of physicians. Ann Intern Med. 2017;166(4):279–90.

116. Caleb Alexander G, Sehgal NL, Moloney RM, Stafford RS. National Trends in Treatment of Type 2 Diabetes Mellitus, 1994-2007. Arch Intern Med. 2008;168(19):2088–94.

117. Fradkin J, Roberts B, Rodgers G. What's Preventing Us from Preventing Type 2 Diabetes? N Engl J Med. 2012;367(13):1177–9.

118. Narayan KMV, Williamson DF. Prevention of Type 2 Diabetes: Risk Status, Clinic, and Community. J Gen Intern Med [Internet]. 2010;25(2):154–7. Available from: http://link.springer.com/10.1007/s11606-009-1148-9

119. Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V. The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). Diabetologia. 2006;49(2):289–97.

120. Tuomilehto J., Indstrom J., Eriksson J., Valle T. HE& UM. Numb Er 18 Prevention of

Type 2 Diabetes Mellitus By Changes in Lifestyle Among Subjects With Impaired Glucose Tolerance. N Engl J Med. 2001;344(18):1343–50.

121. Diabetes Prevention Program Research Group. Reduction in the Incidence of Type 2 Diabetes With Lifestyle Intervention or Metformin. N Engl J Med. 2002;346(6):393–403.

122. Roberts S, Craig D, Adler A, McPherson K, Greenhalgh T. Economic evaluation of type 2 diabetes prevention programmes: Markov model of low- and high-intensity lifestyle programmes and metformin in participants with different categories of intermediate hyperglycaemia. BMC Med. 2018;16(1):1–12.

123. Gregg EW, Boyle JP, Thompson TJ, Barker LE, Albright AL, Williamson DF. Modeling the impact of prevention policies on future diabetes prevalence in the United States: 2010-2030. Popul Health Metr. 2013;11(1):1–9.

124. Rose G. Sick individuals and sick populations. Int J Epidemiol. 2001;30(3):427–32.

125. Imamura F, O'Connor L, Ye Z, Mursu J, Hayashino Y, Bhupathiraju SN, et al. Consumption of sugar sweetened beverages, artificially sweetened beverages, and fruit juice and incidence of type 2 diabetes: systematic review, meta-analysis, and estimation of population attributable fraction. Bmj [Internet]. 2015;h3576. Available from: http://www.bmj.com/lookup/doi/10.1136/bmj.h3576

126. Mcdonald KM, Grimshaw JM, Rushakoff RJ, Owens DK. Effects of Quality Improvement Strategies for Type 2 Diabetes on Glycemic Control. JAMA - J Am Med Assoc. 2006;296(4):427–40.

127. Renders C, Valk G, Griffin S, Wagner E, van Eijk J, Assendelft W. Interventions to improve the management of diabetes mellitus in primary care, outpatient and community settings. Cochrane Database Syst Rev [Internet]. 2000;(4). Available from: https://doi.org//10.1002/14651858.CD001481

128. Zhang J, Donald M, Baxter KA, Ware RS, Burridge L, Russell AW, et al. Impact of an integrated model of care on potentially preventable hospitalizations for people with Type 2 diabetes mellitus. Diabet Med [Internet]. 32(7):872–80. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/dme.12705

129. Nolte E, Knai C, Hofmarcher M, Conklin A, Erler A, Elissen A, et al. Overcoming fragmentation in health care: Chronic care in Austria, Germany and the Netherlands. Heal Econ Policy Law. 2012;7(1):125–46.

130. Fokkens ASS, Wiegersma PAA, Beltman FWW, Reijneveld SAA. Structured primary care for type 2 diabetes has positive effects on clinical outcomes. J Eval Clin Pract. 2011;17(6):1083–8.

131. Welbourn R, le Roux CW, Owen-Smith A, Wordsworth S, Blazeby JM. Why the NHS should do more bariatric surgery; how much should we do?: BMJ [Internet]. 2016;1472(May):i1472. Available from: http://www.bmj.com/lookup/doi/10.1136/bmj.i1472

132. Schauer P, Bhatt D, Kirwan J, Wolski K, Brethauer S, Navaneethan S, et al. Bariatric Surgery versus Intensive Medical Therapy for Diabetes. N Engl J Med [Internet]. 2014;371(7):680–2. Available from: http://www.nejm.org/doi/abs/10.1056/NEJMc1407393%5Cnpapers2://publication/

doi/10.1056/NEJMc1407393

133. Hudson E, Nolan A. Public healthcare eligibility and the utilisation of GP services by older people in Ireland. J Econ Ageing [Internet]. 2015;6:24–43. Available from: http://dx.doi.org/10.1016/j.jeoa.2014.08.005

134. Whelan BJ, Savva GM. Design and methodology of the Irish Longitudinal Study on Ageing. J Am Geriatr Soc. 2013;61(SUPPL2):265–8.

135. Long S, Freese J. Regression Models for Categorical Dependent Variables Using Stata, Revised Edition. 3rd ed. Stata Press; 2014.

136. Williams R. Using the margins command to estimate and interpret adjusted predictions and marginal effects. Stata J [Internet]. 2012;12(2):308–31. Available from: http://ideas.repec.org/a/tsj/stataj/v7y2007i4p465-506.html

137. Andersen R, Newman JF. Societal and individual determinants of medical care utilisation in the United States. Milbank Mem Fund Q. 1973;51(1):95–124.

138. Comptroller and Auditor General. Health Service Executive Emergency Departments [Internet]. 2009. Available from: http://audgen.gov.ie/documents/vfmreports/70_Emergency_Departments.pdf

139. Glynn LG, Valderas JM, Healy P, Burke E, Newell J, Gillespie P, et al. The prevalence of multimorbidity in primary care and its effect on health care utilization and cost. Fam Pract. 2011;28(5):516–23.

140. Central Statistics Office. Consumer Price Index (CPI) Inflation Calculator [Internet]. 2018 [cited 2018 Aug 20]. Available from: https://www.cso.ie/en/interactivezone/visualisationtools/cpiinflationcalculator/

141. HIQA. Health technology assessment of human papillomavirus testing as the primary screening method for prevention of cervical cancer. Heal Inf Qual Auth. 2017;(May):1–347.

142. Kahn R, Anderson JE. Improving diabetes care: The model for health care reform. Diabetes Care. 2009;32(6):1115–8.

143. De Berardis G, D'Ettorre A, Graziano G, Lucisano G, Pellegrini F, Cammarota S, et al. The burden of hospitalization related to diabetes mellitus: A population-based study. Nutr Metab Cardiovasc Dis [Internet]. 2012;22(7):605–12. Available from: http://dx.doi.org/10.1016/j.numecd.2010.10.016

144. Bo S, Ciccone G, Grassi G, Gancia R, Rosato R, Merletti F, et al. Patients with type 2 diabetes had higher rates of hospitalization than the general population. J Clin Epidemiol. 2004;57(11):1196–201.

145. Donnan P, Leese G, Morris A. Hospitalizations for People With Type 1 and Type 2 Diabetes Compared With the Nondiabetic Population of Tayside , Scotland. Diabetes Care. 2000;23(12):1774–9.

146. Riordan F, McHugh SM, Murphy K, Barrett J, Kearney PM. The role of nurse specialists in the delivery of integrated diabetes care: a cross-sectional survey of diabetes nurse specialist services. BMJ Open [Internet]. 2017;7(8):e015049. Available from: http://bmjopen.bmj.com/lookup/doi/10.1136/bmjopen-2016-015049

147. American Diabetes Association (ADA). Standard of medical care in diabetes - 2017. Diabetes Care. 2017;40 (sup 1)(January):s4–128.

148. Li R, Zhang P, Barker LE, Chowdhury FM, Zhang X. Cost-effectiveness of interventions to prevent and control diabetes mellitus: A systematic review. Diabetes Care. 2010;33(8):1872–94.

149. Leahy S, O' Halloran AM, O' Leary N, Healy M, McCormack M, Kenny RA, et al. Prevalence and correlates of diagnosed and undiagnosed type 2 diabetes mellitus and pre-diabetes in older adults: Findings from the Irish Longitudinal Study on Ageing (TILDA). Diabetes Res Clin Pract [Internet]. 2015;110(3):241–9. Available from: http://dx.doi.org/10.1016/j.diabres.2015.10.015

150. Okura Y, Urban LH, Mahoney DW, Jacobsen SJ, Rodeheffer RJ. Agreement between self-report questionnaires and medical record data was substantial for diabetes, hypertension, myocardial infarction and stroke but not for heart failure. J Clin Epidemiol. 2004;57(10):1096–103.

151. Reijneveld S a, Stronks K. The validity of self-reported use of health care across socioeconomic strata: a comparison of survey and registration data. Int J Epidemiol. 2001;30(6):1407–14.

152. Information Unit Department of Health. Long-Stay Activity Statistics 2011 [Internet]. Dublin; 2011. Available from: https://health.gov.ie/wp-content/uploads/2014/03/long_stay_2011.pdf

153. O'Neill K, McHugh S, Tracey M, Fitzgerald A, Kearney P. Health service utilization and related costs attributable to diabetes. Diabet Med [Internet]. 2018;1–8. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/dme.13806?af=R

154. Kearney PM, Cronin H, O'Regan C, Kamiya Y, Savva GM, Whelan B, et al. Cohort profile: The Irish Longitudinal Study on Ageing. Int J Epidemiol. 2011;40(4):877–84.

155. Central Statistics Office. Population estimates from 1926 by single year of age, sex and year [Internet]. 2018 [cited 2018 Sep 9]. Available from: https://www.cso.ie/px/pxeirestat/Statire/SelectVarVal/Define.asp?maintable=PEA11&PLanguage=0

156. Sinnott S-J, Bennett K, Cahir C. Pharmacoepidemiology resources in Ireland-an introduction to pharmacy claims data. Eur J Clin Pharmacol [Internet]. 2017;73(11):1449–55. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28819675%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC5662670

157. HSE. Long Term Illness (LTI) Scheme: Reference Guide as to what is covered in the Health Service Executive for each of the 16 scheduled LTI illnesses. 2016;06(December):7–10. Available from: http://www.hse.ie/eng/services/list/1/schemes/lti/aprovmed/

158. Citizens Information. Sate Pension [Internet]. 2018 [cited 2018 Aug 22]. Available from: http://www.citizensinformation.ie/en/social_welfare/social_welfare_payments/older_and_retired_people/state_pension_contributory.html

159. Citizens Information. Retirement age [Internet]. 2018. [cited 2018 Aug 22]. Available

from:
http://www.citizensinformation.ie/en/employment/retirement/older_people_and_working/retirement_age_in_ireland.html

160. Citizens Information. Disability and illness [Internet]. 2018. [cited 2018 Aug 22]. Available from: http://www.citizensinformation.ie/en/social_welfare/social_welfare_payments/disability_and_illness/

161. Hasse T, Pratschke J. The 2011 Pobal HP Deprivation Index for Small Areas (SA) Introduction and Reference Tables [Internet]. 2012. Available from: https://www.pobal.ie/app/uploads/2018/06/The-2016-Pobal-HP-Deprivation-Index-Introduction-07.pdf

162. Riordan F, McHugh SM, Harkins V, Marsden P, Fitzgerald AP, Kearney PM. A 16-year follow-up study of all-cause mortality among people with diabetes enrolled in a structured primary care diabetes programme. Diabet Med. 2018;IN PRESS.

163. HealthWell. Mortality: Age-specific numbers and rates, national data [Internet]. [cited 2018 Aug 20]. Available from: http://data.thehealthwell.info/NTI/indicators/tables.php?resID=2073

164. Central Statistics Office. StatBank Ireland - Quarterly National Household Survey Main Results [Internet]. 2013 [cited 2018 Sep 13]. Available from: https://www.cso.ie/px/pxeirestat/Database/eirestat/Quarterly National Household Survey Main Results/Quarterly National Household Survey Main Results_statbank.asp?SP=Quarterly National Household Survey Main Results&Planguage=0

165. Dee A, Callinan A, Doherty E, O'Neill C, McVeigh T, Sweeney MR, et al. Overweight and obesity on the island of Ireland: an estimation of costs. BMJ Open. 2015;5(3):e006189–e006189.

166. Peters AL. "Really Good" New Guidelines for T2 Diabetes [Internet]. Medscape Public Health. 2018 [cited 2018 Aug 2]. Available from: https://www.medscape.com/viewarticle/899120?src=mkm_ret_180730_mscpmrk_eumonthly_int&uac=118405AK&impID=1697337&faf=1

167. Lee IH, Bloor K, Hewitt C, Maynard A. International experience in controlling pharmaceutical expenditure: Influencing patients and providers and regulating industry – a systematic review. J Heal Serv Res Policy. 2015;20(1):52–9.

168. OECD. Health at a glance 2015 - How does Ireland compare? 2015;2015:202. Available from: http://www.oecd-ilibrary.org/social-issues-migration-health/health-at-a-glance-2009_health_glance-2009-en

169. Kenneally M, Walshe V. Pharmaceutical cost-containment policies and sustainability: Recent Irish experience. Value Heal [Internet]. 2012;15(2):389–93. Available from: http://dx.doi.org/10.1016/j.jval.2011.10.007

170. Barry M, Usher C, Tilson L. Public drug expenditure in the Republic of Ireland. Expert Rev Pharmacoecon Outcomes Res. 2010;239–45.

171. European Commission. Economic Adjustment Programme for Ireland Autumn 2012 Review [Internet]. 2013. Available from:

http://ec.europa.eu/economy_finance/publications/occasional_paper/2013/pdf/ocp127_en.pdf

172. Usher C, Tilson L, Bennett K, Barry M. Cost containment interventions introduced on the community drugs schemes in Ireland-evaluation of expenditure trends using a national prescription claims database. Clin Ther [Internet]. 2012;34(3):632–9. Available from: http://dx.doi.org/10.1016/j.clinthera.2012.01.025

173. Drummond M, Towse A. Is it time to reconsider the role of patient co-payments for pharmaceuticals in Europe? Eur J Heal Econ. 2012;13(1):1–5.

174. Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D. Segmented regression analysis of interrupted time series studies in medication use research. J Clin Pharm Ther [Internet]. 2002;27(4):299–309. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12174032

175. Bernal JL, Cummins S, Gasparrini A. Interrupted time series regression for the evaluation of public health interventions: A tutorial. Int J Epidemiol. 2017;46(1):348–55.

176. Department of Health. Reference Pricing [Internet]. 2014 [cited 2018 Jun 13]. Available from: https://health.gov.ie/future-health/reforming-primary-care-2/reference-pricing/

177. Currie CJ, Peters JR, Evans M. Dispensing patterns and financial costs of glucose-lowering therapies in the UK from 2000 to 2008. Diabet Med. 2010;27(7):744–52.

178. Inzucchi SE, Bergenstal RM, Buse JB, Diamant M, Ferrannini E, Nauck M, et al. Management of Hyperglycemia in Type 2 Diabetes, 2015: A Patient-Centered Approach: Update to a position statement of the american diabetes association and the european association for the study of diabetes. Diabetes Care. 2015;38(1):140–9.

179. McCoy RG, Zhang Y, Herrin J, Denton BT, Mason JE, Montori VM, et al. Changing trends in type 2 diabetes mellitus treatment intensification, 2002-2010. Am J Manag Care [Internet]. 2015;21(5):e288-96. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26167776

180. Torre C, Guerreiro J, De Oliveira Martins S, Raposo JF, Martins AP, Leufkens H. Patterns of glucose lowering drugs utilization in Portugal and in the Netherlands. Trends over time. Prim Care Diabetes [Internet]. 2015;9(6):482–9. Available from: http://dx.doi.org/10.1016/j.pcd.2015.03.009

181. Overbeek JA, Heintjes EM, Prieto-Alhambra D, Blin P, Lassalle R, Hall GC, et al. Type 2 Diabetes Mellitus Treatment Patterns Across Europe: A Population-based Multi-database Study. Clin Ther. 2017;39(4):759–70.

182. Prescribing and Medicines Team NHS Digital. Prescribing for Diabetes England 2006/07 to 2016/17. Can Med Assoc J. 2017;(August):1–24.

183. Śliwczyñski A, Brzozowska M, Jacyna A, Iltchev P, Iwañczuk T, Wierzba W, et al. Drug-class-specific changes in the volume and cost of antidiabetic medications in Poland between 2012 and 2015. PLoS One. 2017;12(6):1–11.

184. Grimes RT, Bennett K, Canavan R, Tilson L, Henman MC. The impact of initial antidiabetic agent and use of monitoring agents on prescription costs in newly

treated type 2 diabetes: A retrospective cohort analysis. Diabetes Res Clin Pract [Internet]. 2016;113:152–9. Available from: http://dx.doi.org/10.1016/j.diabres.2015.12.020

185. National Institute of Health and Care Excellence (NICE). Type 2 diabetes in adults: management. NICE guideline (NG 28) [Internet]. NICE Guidelines. 2015. Available from: https://www.nice.org.uk/guidance/ng28/resources/type-2-diabetes-in-adults-management-1837338615493

186. Lipska KJ, Yao X, Herrin J, McCoy RG, Ross JS, Steinman MA, et al. Trends in drug utilization, glycemic control, and rates of severe hypoglycemia, 2006-2013. Diabetes Care. 2017;40(4):468–75.

187. Patel H, Srishanmuganathan J, Car J, Majeed A. Trends in the prescription and cost of diabetic medications and monitoring equipment in England 1991-2004. J Public Health (Bangkok). 2007;29(1):48–52.

188. Palmer SC, Mavridis D, Nicolucci A, Johnson DW, Tonelli M, Craig JC, et al. Comparison of clinical outcomes and adverse events associated with glucose-lowering drugs in patients with type 2 diabetes a meta-analysis. JAMA. 2016;316(3):313–24.

189. Cohen D. Has pancreatic damage from glucagon suppressing diabetes drugs been underplayed? BMJ. 2013;346(7912):1–11.

190. Butler PC, Elashoff M, Elashoff R, Gale EAM. A Critical Analysis of the Clinical Use of Incretin-Based Therapies. Diabetes Care [Internet]. 2013;36(7):2118–25. Available from: http://care.diabetesjournals.org/content/36/7/2118.abstract

191. Egan AG, Blind E, Dunder K, de Graeff PA, Hummer BT, Bourcier T, et al. Pancreatic Safety of Incretin-Based Drugs — FDA and EMA Assessment. N Engl J Med [Internet]. 2014;370(9):794–7. Available from: http://www.nejm.org/doi/10.1056/NEJMp1400601

192. American Diabetes Association. Standards of Medical Care in Diabetes: Pharmacologic Approaches to Glycemic Treatment. Diabetes Care. 2017;40(Supplement 1):S64–74.

193. Nathan DM, Buse JB, Kahn SE, Krause-Steinrauf H, Larkin ME, Staten M, et al. Rationale and design of the glycemia reduction approaches in diabetes: A comparative effectiveness study (GRADE). Diabetes Care. 2013;36(8):2254–61.

194. Thomas S, Burke S, Barry S. The Irish health-care system and austerity: Sharing the pain. Lancet [Internet]. 2014;383(9928):1545–6. Available from: http://dx.doi.org/10.1016/S0140-6736(14)60744-3

195. Galizzi MM., Ghislandi S, Miraldo M. Effects of Reference Pricing in Pharmaceutical Markets: A Review. Pharmacoeconomics. 2011;29(1):17–33.

196. Medicines Management Programme. Report on Self-Monitoring of Blood Glucose (SMBG) in Type 2 Diabetes Mellitus. 2016;(October 2014). Available from: http://www.hse.ie/eng/about/Who/clinical/natclinprog/medicinemanagementprogramme/yourmedicines/Evaluation_Reports/selfmonitoringbloodglucosetype2.pdf

197. Pate KA. Epidemiology , diagnosis , and management of polycystic ovary syndrome. Clin Epidemiol. 2014;6:1–13.

198. Backholer K, Blake M, Vandevijvere S. Sugar-sweetened beverage taxation: An update on the year that was 2017. Public Health Nutr. 2017;20(18):3219–24.

199. Manyema M, Veerman JL, Chola L, Tugendhaft A, Labadarios D, Hofman K. Decreasing the burden of type 2 diabetes in South Africa: The impact of taxing sugar-sweetened beverages. PLoS One. 2015;10(11):1–17.

200. Barrientos-Gutierrez T, Zepeda-Tello R, Rodrigues ER, Colchero-Aragones A, Rojas-Martõnez R, Lazcano-Ponce E, et al. Expected population weight and diabetes impact of the 1-peso-per-litre tax to sugar sweetened beverages in Mexico. PLoS One. 2017;12(5):1–15.

201. Veerman JL, Sacks G, Antonopoulos N, Martin J. The impact of a tax on sugar-sweetened beverages on health and health care costs: A modelling study. PLoS One. 2016;11(4):1–10.

202. Sánchez-Romero LM, Penko J, Coxson PG, Fernández A, Mason A, Moran AE, et al. Projected Impact of Mexico's Sugar-Sweetened Beverage Tax Policy on Diabetes and Cardiovascular Disease: A Modeling Study. PLoS Med. 2016;13(11):1–17.

203. Briggs ADM, Mytton OT, Kehlbacher A, Tiffin R, Elhussein A, Rayner M, et al. Health impact assessment of the UK soft drinks industry levy: a comparative risk assessment modelling study. Lancet Public Heal [Internet]. 2017;2(1):e15-22. Available from: http://linkinghub.elsevier.com/retrieve/pii/S2468266716300378

204. Darrow LA, Steenland NK. Confounding and bias in the attributable fraction. Epidemiology. 2011;22(1):53–8.

205. Steenland K, Armstrong B. An Overview of Methods for Calculating the Burden of Disease Due to Specific Risk Factors. Epidemiology [Internet]. 2006;17(5):512–9. Available from: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00001648-200609000-00008

206. Flegal KM. Bias in calculation of attributable fractions using relative risks from non-smokers only. Epidemiology. 2014;25(6):913–6.

207. Basu S, Vellakkal S, Agrawal S, Stuckler D, Popkin B, Ebrahim S. Averting Obesity and Type 2 Diabetes in India through Sugar-Sweetened Beverage Taxation: An Economic-Epidemiologic Modeling Study. PLoS Med. 2014;11(1):1–2.

208. Mekonnen TA, Odden MC, Coxson PG, Guzman D, Lightwood J, Wang YC, et al. Health benefits of reducing sugar-sweetened beverage intake in high risk populations of California: Results from the Cardiovascular Disease (CVD) policy model. PLoS One. 2013;8(12):1–9.

209. Collins B, Capewell S, O'Flaherty M, Timpson H, Razzaq A, Cheater S, et al. Modelling the health impact of an English sugary drinks duty at national and local levels. PLoS One. 2015;10(6):1–13.

210. Briggs AD, Mytton OT, Madden D, O'Shea D, Rayner M, Scarborough P. The potential impact on obesity of a 10% tax on sugar-sweetened beverages in Ireland, an effect assessment modelling study. BMC Public Health [Internet]. 2013;13(1):860. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3852031&tool=pmcent

rez&rendertype=abstract

211. Singh GM, Micha R, Khatibzadeh S, Lim S, Ezzati M, Mozaffarian D. Estimated global, regional, and national disease burdens related to sugar-sweetened beverage consumption in 2010. Circulation. 2015;132(8):639–66.

212. Rockhill B, Newman B, Weinberg C. Use and misuse of population attributable fractions. Am J Public Health. 1998;88(1):15–9.

213. Flegal KM, Panagiotou OA, Graubard BI. Estimating population attributable fractions to quantify the health burden of obesity. Ann Epidemiol [Internet]. 2015;25(3):201–7. Available from: http://dx.doi.org/10.1016/j.annepidem.2014.11.010

214. Malik VS, Popkin BM, Bray GA, Despres JP, Willett WC, Hu FB. Sugar-sweetened beverages and risk of metabolic syndrome and type 2 diabetes: a meta-analysis. Diabetes Care. 2010;33(11):2477–81.

215. Barendregt JJ, Veerman JL. Categorical versus continuous risk factors and the calculation of potential impact fractions. J Epidemiol Community Heal [Internet]. 2010;64(3):209–12. Available from: http://jech.bmj.com/cgi/doi/10.1136/jech.2009.090274

216. Benichou J. A review of adjusted estimators of attributable risk. Stat Methods Med Res [Internet]. 2001;10(3):195–216. Available from: http://journals.sagepub.com/doi/10.1177/096228020101000303

217. Morgan K, McGee H, Watson D, Perry I. SLAN 2007: survey of lifestyle, attitudes & nutrition in Ireland: main report [Internet]. 2008. Available from: http://epubs.rcsi.ie/cgi/viewcontent.cgi?article=1002&context=psycholrep

218. Harrington J, Lutomski J, Mcgee H. SLAN 2007: Survey of Lifestyle , Attitudes and Nutrition in Ireland . Dietary Habits of the Irish Population [Internet]. 2008. Available from: https://epubs.rcsi.ie/cgi/viewcontent.cgi?article=1005&context=psycholrep

219. Hippisley-Cox J, Coupland C, Robson J, Sheikh A, Brindle P. Predicting risk of type 2 diabetes in England and Wales: prospective derivation and validation of QDScore. Br Med J [Internet]. 2009;338:b880–b880. Available from: http://www.bmj.com/cgi/content/abstract/338/mar17_2/b880

220. Scott RA, Langenberg C, Sharp SJ, Franks PW, Rolandsson O, Drogan D, et al. The link between family history and risk of type 2 diabetes is not explained by anthropometric, lifestyle or genetic risk factors: The EPIC-InterAct study. Diabetologia. 2013;56(1):60–9.

221. Haase T, Pratschke J, Gleeson J. The 2011 All Island HP Deprivation Index Ireland , based on the 2011 Census of Deprivation. 2014.

222. Cabrera Escobar MA, Veerman JL, Tollman SM, Bertram MY, Hofman KJ. Evidence that a tax on sugar sweetened beverages reduces the obesity rate: a meta-analysis. BMC Public Health [Internet]. 2013;13(1):1072. Available from: http://bmcpublichealth.biomedcentral.com/articles/10.1186/1471-2458-13-1072

223. Gmel GG, Shield KD, Frick H, Kehoe T, Gmel GG, Rehm J. Estimating uncertainty of alcohol-attributable fractions for infectious and chronic diseases. BMC Med Res Methodol [Internet]. 2011;11(1):48. Available from: http://www.biomedcentral.com/1471-2288/11/48

224. Greenland S. Interval estimation by simulation as an alternative to and extension of confidence intervals. Int J Epidemiol. 2004;33(6):1389–97.

225. Shim J-S, Oh K, Kim HC. Dietary assessment methods in epidemiologic studies. Epidemiol Health [Internet]. 2014;e2014009. Available from: http://e-epih.org/journal/view.php?doi=10.4178/epih/e2014009

226. Flegal KM, Graubard BI, Williamson DF. Methods of calculating deaths attributable to obesity. Am J Epidemiol. 2004;160(4):331–8.

227. Brownell KD, Farley T, Willett WC, Popkin BM, Chaloupka FJ, Thompson JW, et al. The Public Health and Economic Benefits of Taxing Sugar-Sweetened Beverages. N Engl J Med. 2009;361(16):1599–605.

228. Quirmbach D, Cornelsen L, Jebb SA, Marteau T, Smith R. Effect of increasing the price of sugar-sweetened beverages on alcoholic beverage purchases: an economic analysis of sales data. J Epidemiol Community Health [Internet]. 2018;jech-2017-209791. Available from: http://jech.bmj.com/lookup/doi/10.1136/jech-2017-209791

229. Colchero MA, Popkin BM, Rivera JA, Ng SW. Beverage purchases from stores in Mexico under the excise tax on sugar sweetened beverages: Observational study. BMJ [Internet]. 2016;352:1–9. Available from: http://www.bmj.com/lookup/doi/10.1136/bmj.h6704

230. Rutter H, Savona N, Glonti K, Bibby J, Cummins S, Finegood DT, et al. The need for a complex systems model of evidence for public health. Lancet [Internet]. 2017;390(10112):2602–4. Available from: http://dx.doi.org/10.1016/S0140-6736(17)31267-9

231. Kearney PM, Cronin H, O'Regan C, Kamiya Y, Savva GM, Whelan B, et al. Cohort Profile: The Irish Longitudinal Study on Ageing. Int J Epidemiol. 2011;40:877–84.

232. Comino EJ, Tran DT, Haas M, Flack J, Jalaludin B, Jorm L, et al. Validating self-report of diabetes use by participants in the 45 and up study: a record linkage study. BMC Health Serv Res [Internet]. 2013;13(1):481. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24245780

233. Basterra-gortari FJ, Beunza JJ, Bes-Rastrollo M, Teledo E, Garcia-Lopez M, Martınez-Gonzalez MA. Increasing Trend in the Prevalence of Morbid Obesity in Spain : From 1 . 8 to 6 . 1 per Thousand in 14 Years. Rev Esp Cardiol. 2011;64(5):424–6.

234. Sturm R, Hattori A. Morbid obesity rates continue to rise rapidly in the United States. Int J Obes (Lond) [Internet]. 2013;37(6):889–91. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22986681%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC3527647

235. Finucane MM, Stevens GA, Cowan MJ, Danaei G, Lin JK, Paciorek CJ, et al. National, regional, and global trends in body-mass index since 1980: Systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. Lancet [Internet]. 2011;377(9765):557–67. Available from: http://dx.doi.org/10.1016/S0140-6736(10)62037-5

236. Papasavas P, El Chaar M, Kothari SN. American Society for Metabolic and Bariatric Surgery position statement on vagal blocking therapy for obesity. Surg Obes Relat

Dis [Internet]. 2016;12(3):460–1. Available from: http://dx.doi.org/10.1016/j.soard.2015.11.021

237. Rubino F, Nathan DM, Eckel RH, Schauer PR, Alberti KGMM, Zimmet PZ, et al. Metabolic surgery in the treatment algorithm for type 2 diabetes: A joint statement by international diabetes organizations. Diabetes Care. 2016;39(7):861–77.

238. Colquitt JL, Pickett K, Loveman E, Frampton GK. Surgery for weight loss in adults. Cochrane database Syst Rev [Internet]. 2014;8(8):CD003641. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25105982

239. Sjöström L. Review of the key results from the Swedish Obese Subjects (SOS) trial - a prospective controlled intervention study of bariatric surgery. J Intern Med. 2013;273(3):219–34.

240. Adams TD, Gress RE, Smith SC, Halverson RC, Simper SC, Rosamond WD, et al. Long-term mortality after gastric bypass surgery. N Engl J Med [Internet]. 2007;357(8):753–61. Available from: /Users/EWN/Documents/Arkiv_artikler/6500_6599/6522.pdf

241. Welbourn R, Small P, Finlay I, Sareela A, Somers S, Mahawar K. The United Kingdom National Bariatric Surgery Registry Second Report [Internet]. Oxfordshire: Dendrite Clinical Systems Ltd; 2014. Available from: papers2://publication/uuid/315BEF18-52C2-4FF2-81D5-721662463DE0

242. Picot J, Jones J, Colquitt JL, Gospodarevskaya E, Loveman E, Baxter L, et al. The clinical effectiveness and cost-effectiveness of bariatric (weight loss) surgery for obesity: a systematic review and economic evaluation. Health Technol Assess. 2009;13(41).

243. Klein S, Ghosh A, Cremieux PY, Eapen S, McGavock TJ. Economic impact of the clinical benefits of bariatric surgery in diabetes patients with BMI ≥35 kg/m^2. Obesity [Internet]. 2011;19(3):581–7. Available from: http://dx.doi.org/10.1038/oby.2010.199/nature06264

244. Keating CL, Dixon JB, Moodie ML, Peeters A, Buflone L, Maglianno DJ, et al. Cost-Effectiveness of Surgically Induced Weight Loss for the Management of Type 2 Diabetes : Modeled Lifetime Analysis. Diabetes Care. 2009;32(4):567–74.

245. Angrisani L, Santonicola A, Iovino P, Formisano G, Buchwald H, Scopinaro N. Bariatric Surgery Worldwide 2013. Obes Surg. 2015;25(10):1822–32.

246. Buchwald H, Oien DM. Metabolic/bariatric surgery worldwide 2011. Obes Surg. 2013;23(4):427–36.

247. OECD. Health at a Glance : Europe 2014 [Internet]. OECD Publishing; 2014. Available from: http://dx.doi.org/10.1787/health_glance_eur-2014-en

248. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep. 1991;14(6):540–5.

249. Punjabi NM. The epidemiology of adult obstructive sleep apnea. Proc Am Thorac Soc [Internet]. 2008;5(2):136–43. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2645248&tool=pmcentrez&rendertype=abstract

250. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: A population health perspective. Am J Respir Crit Care Med. 2002;165(9):1217–39.

251. Welsh JA, Lundeen EA, Stein AD. The sugar-sweetened beverage wars: Public health and the role of the beverage industry. Curr Opin Endocrinol Diabetes Obes. 2013;20(5):401–6.

252. Pomeranz JL. Advanced policy options to regulate sugar-sweetened beverages to support public health. J Public Health Policy. 2012;33(1):75–88.

253. Department of Health I. Future Health A Strategic Framework for Reform of the Health Service 2012 – 2015 Department of Health. Dep Heal Irel. 2012;(November 2012):1–61.

254. Grimes RT, Ensor J, Bennett K, Henman MC. Use of cardiovascular medicines in newly treated type 2 diabetes patients: A retrospective cohort study in general practice. Prim Care Diabetes [Internet]. 2015;1–7. Available from: http://dx.doi.org/10.1016/j.pcd.2015.11.002

255. Grimes RT, Bennett K, Tilson L, Usher C, Smith SM, Henman MC. Initial therapy, persistence and regimen change in a cohort of newly treated type 2 diabetes patients. Br J Clin Pharmacol. 2015;79(6):1000–9.

11. Appendices

Appendix 1 – Supplementary Data for Chapter 3

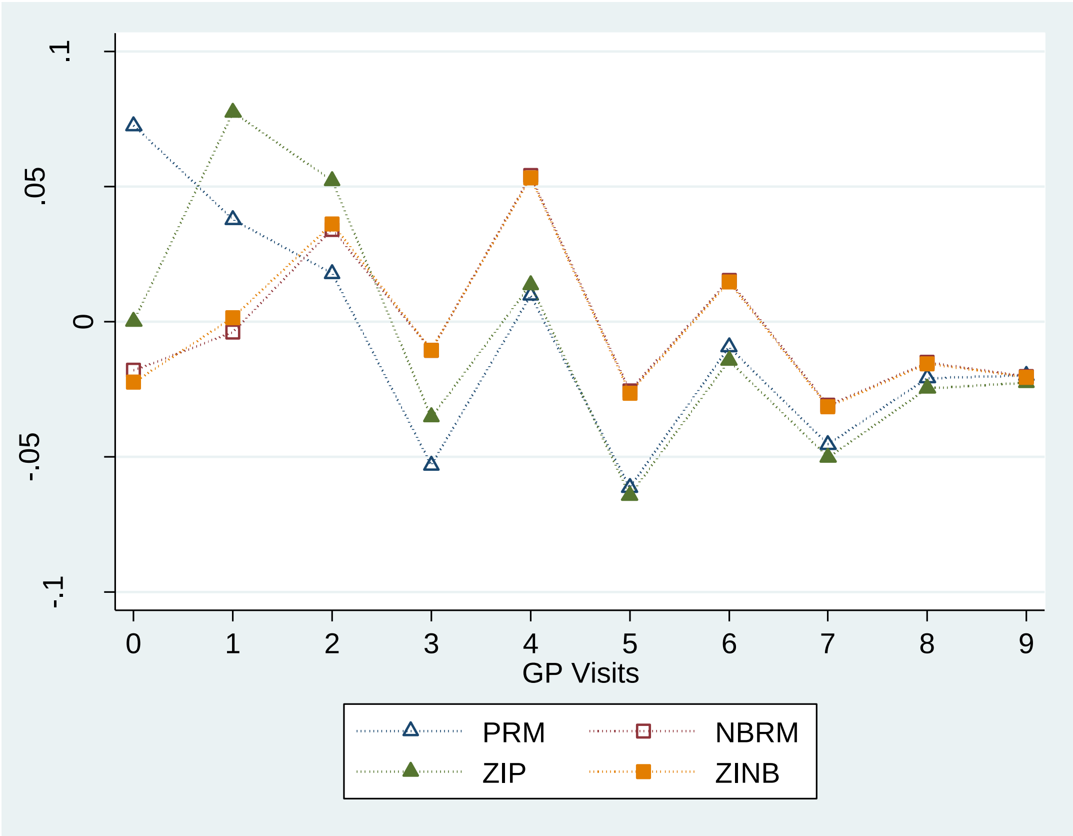
Table S1 – Evidence for Model Selection

	Poisson	Negative Binomial	Zero-inflated Poisson	Zero-inflated Negative Binomial
GP visits				
AIC	44973.985	37896.424	43761.648	37876.907
BIC	45057.991	37987.430	43929.660	38051.919
Mean difference between observed and predicted count	0.035	0.023	0.036	0.023
Out-patient department				
AIC	30296.569	22843.915	24775.994	22694.836
BIC	30380.574	22934.921	24944.006	22869.849
Mean difference between observed and predicted count	0.057	0.005	0.020	0.005
Hospital admission				
AIC	9031.183	8034.123	8209.350	8203.378
BIC	9115.189	8125.129	8377.361	8028.366
Mean difference between observed and predicted count	0.012	0.002	0.004	0.002
A&E attendance				
AIC	9999.863	8986.221	9191.499	8986.277
BIC	10083.869	9077.227	9359.510	9161.289
Mean difference between observed and predicted count	0.013	0.002	0.004	0.002

AIC - Akaike Information Criterion

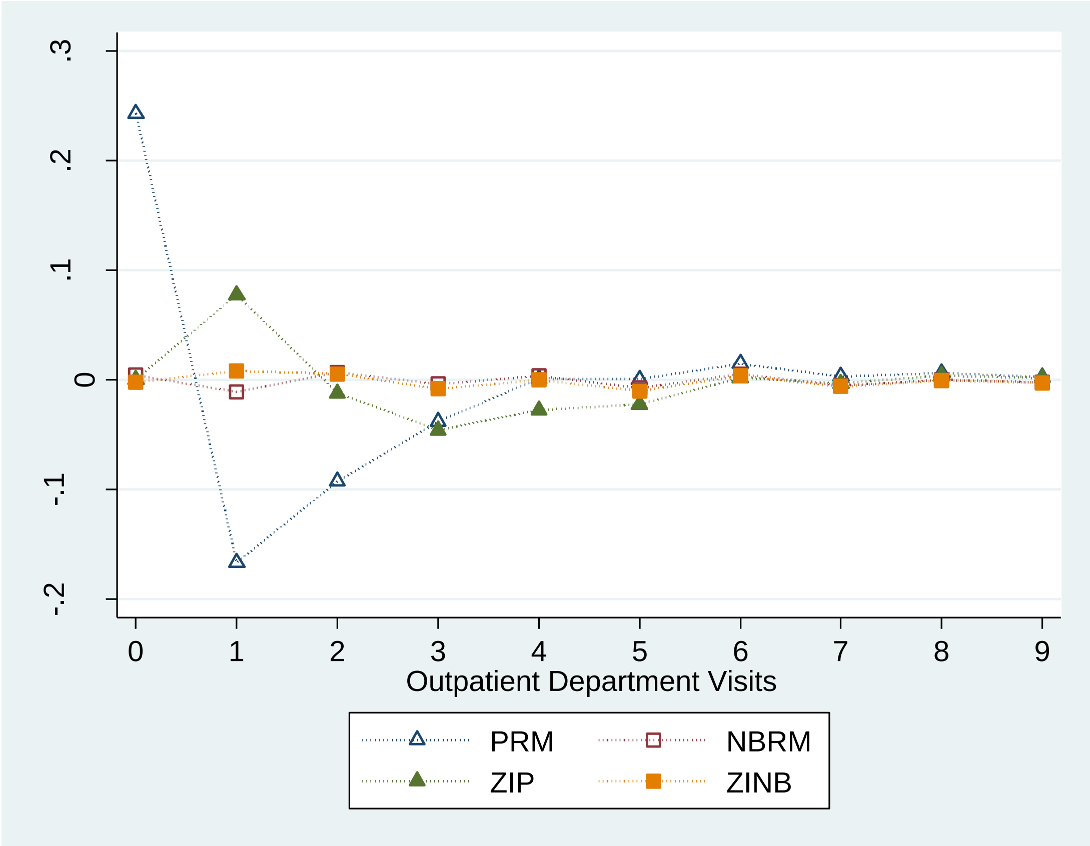
BIC - Bayesian Information Criterion

Figure S1 – Residual plot: GP visits per annum



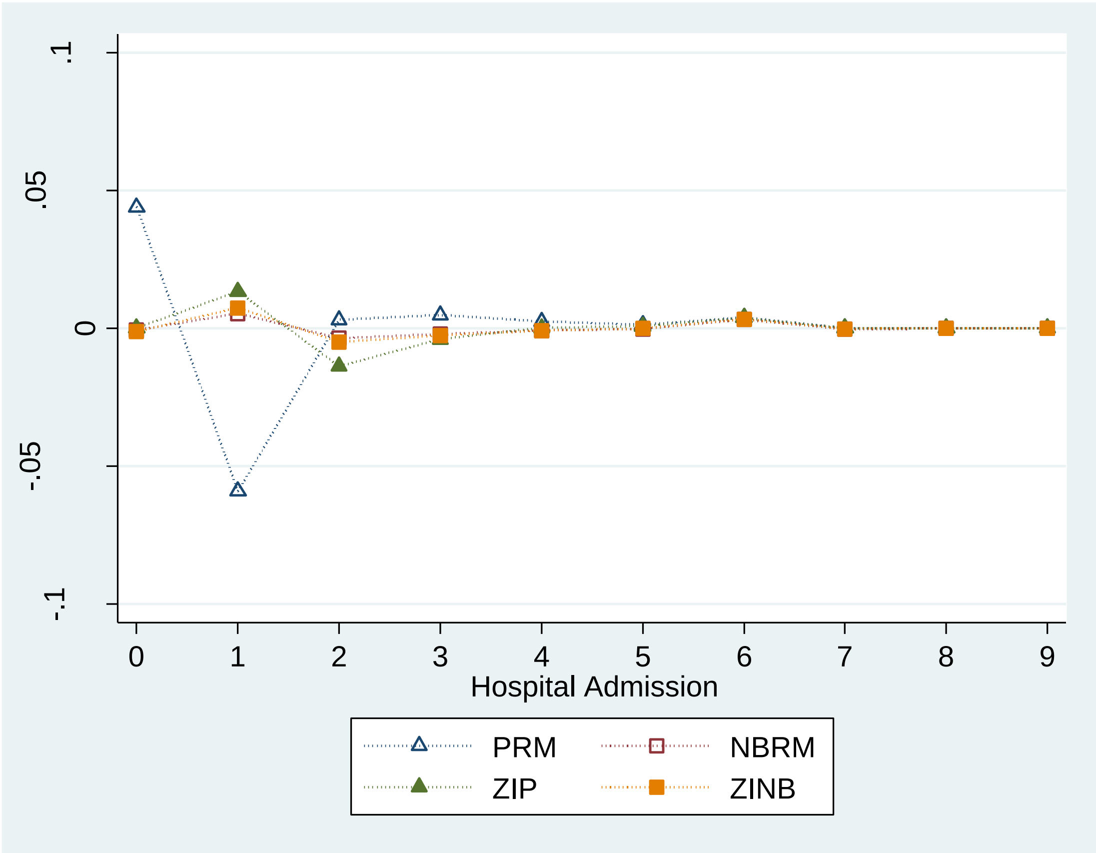
PRM – Poisson Model
NBRM – Negative Binomial Model
ZIP – Zero-inflated Poisson Model
ZINB – Zero-inflated Negative Binomial Model

Figure S2 – Residual plot: Outpatient department visits per annum



PRM – Poisson Model
NBRM – Negative Binomial Model
ZIP – Zero-inflated Poisson Model
ZINB – Zero-inflated Negative Binomial Model

Figure S3 – Residual plot: Hospital admissions per annum



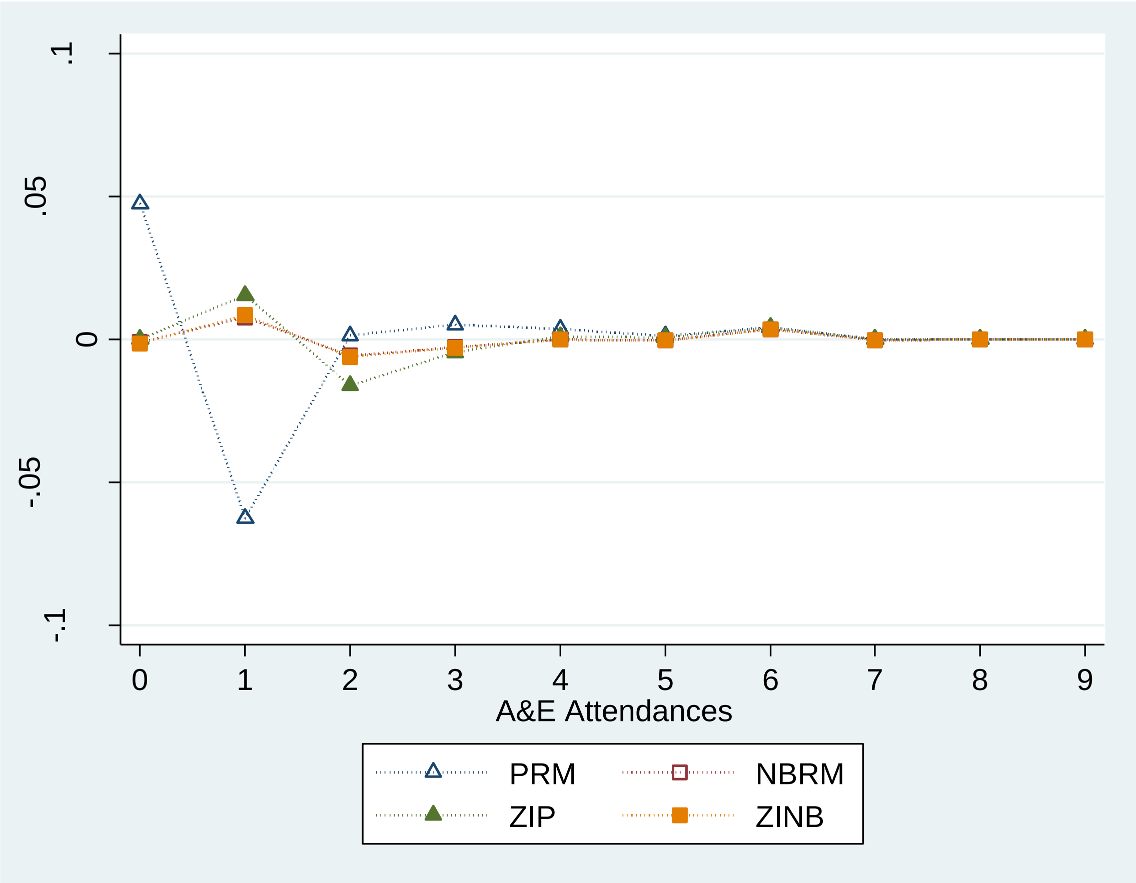
PRM – Poisson Model

NBRM – Negative Binomial Model

ZIP – Zero-inflated Poisson Model

ZINB – Zero-inflated Negative Binomial Model

Figure S4 – Residual plot: A&E attendances per annum



PRM – Poisson Model
NBRM – Negative Binomial Model
ZIP – Zero-inflated Poisson Model
ZINB – Zero-inflated Negative Binomial Model

Appendix 2 – Supplementary Data for Chapter 5

Diabetes-specific items	Other items
Drugs used in diabetes A10	**Antithrombotic agents – B01**
Insulins – A10A	Warfarin - B01AA03
1. A10AB01	Clopidogrel - B01AC04
2. A10AB04	Acetylsalicylic Acid – B01AC06 (*Aspirin - Antithrombotic)
3. A10AB05	Dabigatran Etexilate – B01AE07
4. A10AB06	Apixaban – B01AF02
5. A10AC01	Rivaroxaban – B01AF01
6. A10AD01	Edoxaban – B01AF03
7. A10AD05	
8. A10AD30	**Cardiovascular system - C**
9. A10AE01	**Cardiac therapy – C01**
10. A10AE04	Glyceryl Trinitrate - C01DA02
11. A10AE05	Isosorbide Dinitrate – C01DA08
12. A10AE06	Isosorbide Mononitrate – C01DA14
Blood glucose-lowering drugs – A10B	
Metformin – A10BA02	**Antihypertensives – C02**
Glibenclamide – A10BB01	Methyldopa – C02AB01
Glicazide – A10BB09	Clonidine – C02AC01
Glimepiride – A10BB12	Prazosin – C02CA01
Metformin and Pioglitazone – A10BD05	Indoramin – C02CA02
Metformin and Sitaliptin – A10BD07	Doxazosin – C02CA04
Metformin and Vildagliptin – A10BD08	Hydralazine – C02DB02
Metformin and Saxagliptin – A10BD10	Minoxidil – C02DC01
Metformin and Linagliptin – A10BD11	
Metformin and Dapaglifozin – A10BD15	**Diuretics – C03**
Metformin and Canagliflozin – A10BD16	Bendroflumethiazide – C03AA01
Metformin and Empagliflozin – A10BD20	Bendroflumethiazide and Potassium – C03AB01 Xipamide – C03BA10
Acarbose – A10BF01	Indapamide – C03BA11
Pioglitazone – A10BG03	Furosemide – C03CA01
Sitagliptin – A10BH01	Bumetanide – C03CA02
Vildagliptin – A10BH02	Piretanide – C03CA03
Saxagliptin – A10BH03	Spironolactone – C03DA01
Linagliptin – A10BH05	Eplerenone – C03DA04
Canagliflozin – A10BK02	Hydrochlorothiazide & Potassium Sparing Agents – C03EA01
Repaglinide – A10BX02	
Nateglinide – A10BX03	Furosemide & Potassium Sparing Agents – C03EB01
Exenatide – A10BJ01	
Liraglutide – A10BJ02	
Dapafliglozin – A10BK01	**Beta blocking agents – C07**
Empagliflozin - A10BK03	Propranolol – C07AA05
Dulaglutide – A10BJ05	Sotalol – C07AA07
Diagnostic agents – V04	Metoprolol – C07AB02
	Atenolol – C07AB03

Blood glucose/Ketones test strips, urine test strips etc., (but not Meters) – V04

All other non-therapeutic agents – V07
Insulin needles and syringes – V07
Lancets – V07
Dextrose Gel
Injection swabs
Control solutions for use with meters.
Infusion sets and appliances required for use with Insulin pumps (e.g. Medtronic Minimed Sets, though not the actual Insulin Pumps) – V07
Consumable Items required for use with Insulin Pumps
Batteries for Insulin Pumps - V07AY92

Bisoprolol – C07AB07
Celiprolol – C07AB08
Nebivolol – C07AB12
Labetalol – C07AG01
Carvedilol – C07AG02
Timolol and Thiazides – C07BA06
Nebivolol and Thiazides – C07BB12
Atenolol and other Diuretics – C07CB03
Atenolol and other Antihypertensives – C07FB03

Calcium channel blockers – C08
Amlodipine – C08CA01
Felodipine – C08CA02
Nifedipine – C08CA05
Nimodipine – C08CA06
Nilvadipine – C08CA10
Lercanidipine – C08CA13
Verapamil – C08DA01
Diltiazem – C08DB01

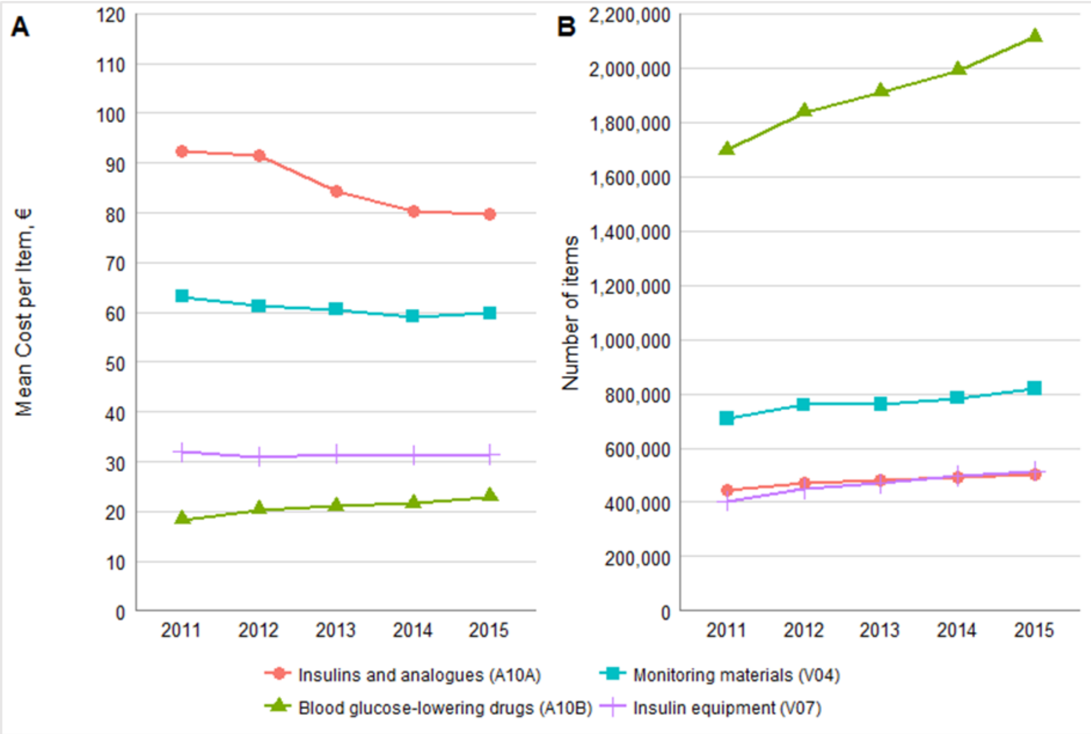
Agents acting on the renin-angiotensin system – C09
Captopril – C09AA01
Enalapril – C09AA02
Lisinopril – C09AA03
Perindopril – C09AA04
Ramipril – C09AA05
Quinapril – C09AA06
Benazepril – C09AA07
Cilazapril – C09AA08
Trandolapril – C09AA10
Zofenopril – C09AA15
Captopril and Diuretics – C09BA01
Enalapril and Diuretics – C09BA02
Lisinopril and Diuretics – C09BA03
Perindopril and Diuretics – C09BA04
Ramipril and Diuretics – C09BA05
Quinapril and Diuretics – C09BA06
Enalapril and Lercanidipine – C09BB02
Perindopril and Amlodipine – C09BB04
Ramipril and Felodipine – C09BB05
Perindopril, Amlodipine and Indapamide – C09BX01
Perindopril and Bisoprolol – C09BX02
Losartan – C09CA01
Eprosartan – C09CA02
Valsartan – C09CA03
Irbesartan – C09CA04
Candesartan – C09CA06

Telmisartan – C09CA07
Olmesartan Medoxomil – C09CA08
Azilsartan Medoxomil – C09CA09
Losartan and Diuretics – C09DA01
Eprosartan and Diuretics – C09DA02
Valsartan and Diuretics – C09DA03
Irbesartan and Diuretics – C09DA04
Candesartan and Diuretics – C09DA06
Telmisartan and Diuretics – C09DA07
Olmesartan Medoxomil and Diuretics – C09DA08
Valsartan and Amlodipine – C09DB01
Olmesartan Medoxomil & Amlodipine – C09DB02
Telmisartan and Amlodipine – C09DB04
Valsartan, Amlodipine & Hydrochlorothiazide – C09DX01
Olmesartan Medoxomil, Amlodipine & Hydrochlorothiazide – C09DX03
Aliskiren – C09XA02
Aliskiren and Hydrochlorothiazide – C09XA52

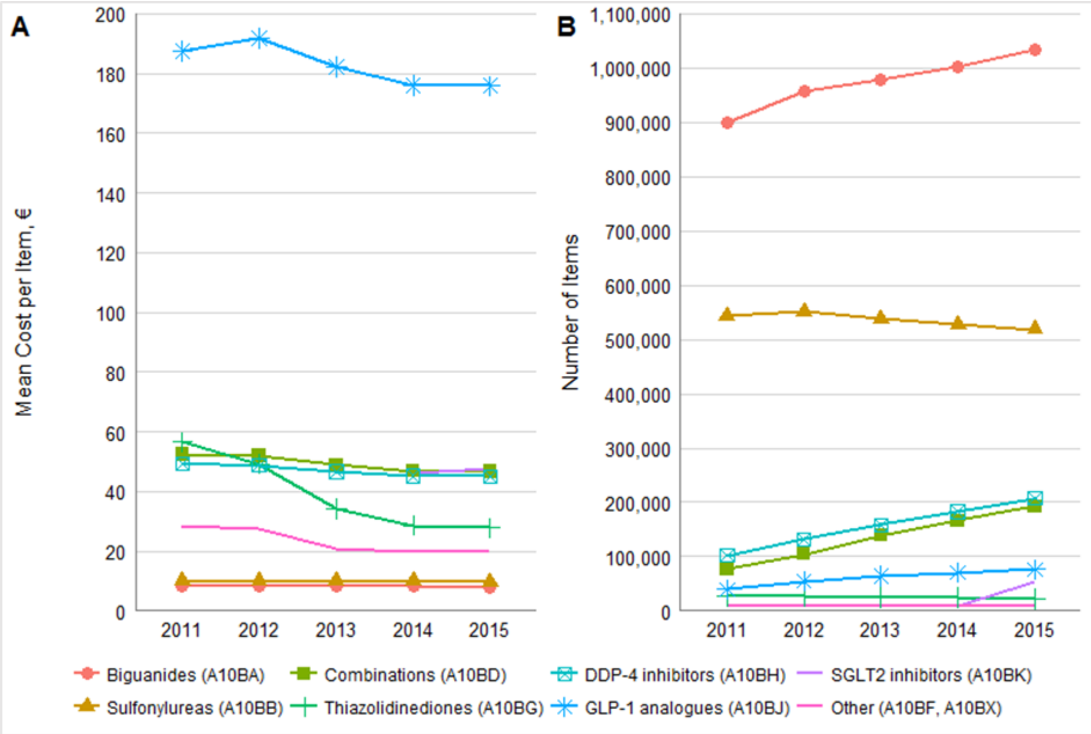
Lipid modifying agents – C10
Simvastatin – C10AA01
Pravastatin – C10AA03
Fluvastatin – C10AA04
Atorvastatin – C10AA05
Rosuvastatin – C10AA07
Gemfibrozil – C10AB04
Fenofibrate – C10AB05
Colestyramine – C10AC01
Colesevelam – C10AC04
Ezetimibe – C10AX09
Simvastatin and Ezetimibe – C10BA02
Atorvastatin and Ezetimibe – C10BA05
Atorvastatin, Acetylsalicylic Acid and Ramipril – C10BX06

Other
Glucagen Hypokit. – H04AA01
Gabapentin - N03AX12
Amitriptyline – N06AA09

Supplementary Figure 1 - Trends in (A) average prescription costs and (B) number of items, 2011-2015



Supplementary Figure 2 - Trends in (A) average prescription costs and (B) number of items, 2011-2015



Appendix 3 – Research Output and Dissemination

A.3.1 Peer-reviewed publications

Year	Publication
2018	**O'Neill KN**, McHugh SM, Tracey ML, Fitzgerald AP, Kearney PM. Health service utilization and related costs attributable to diabetes. Diabetic Med 2018:1–8. doi:10.1111/dme.13806.
2017	**O'Neill KN**, Finucane FM, le Roux CW, Fitzgerald AP, Kearney PM. Unmet need for bariatric surgery. Surg Obes Relat Dis 2017;13:1052–6. doi:10.1016/j.soard.2016.12.015.
2016	Tracey ML, Gilmartin M, **O'Neill K**, Fitzgerald AP, McHugh SM, Buckley CM, et al. Epidemiology of diabetes and complications among adults in the Republic of Ireland 1998-2015: a systematic review and meta-analysis. BMC Public Health. 2016;16(1):1-13.
2015	McHugh S, Tracey ML, Riordan F, **O'Neill K**, Mays N, Kearney PM. Evaluating the implementation of a national clinical programme for diabetes to standardise and improve services: a realist evaluation protocol. **Implementation Science**: IS. 2015;11:107.

A3.2 Conference Presentations

Year	Title		Conference
2018	Impact of Population Shifts in Sugar Sweetened Beverage Consumption on Type 2 Diabetes Incidence: A Comparative Risk Assessment Study	Oral	European Congress of Epidemiology, Lyon, July 2018
2018	Trends in Diabetes-related Prescription Costs in Ireland	Oral	SPHeRE Network Annual Conference, Dublin, January 2018
2017	Impact of Sugar Sweetened Beverage Consumption on Type 2 Diabetes Incidence in Ireland	Oral	Jacqueline Horgan Bronze Medal Meeting, Dublin,
2017	Impact of Sugar-Sweetened Beverages on Type 2 Diabetes Incidence in Ireland	Poster	World Congress of Epidemiology, Saitima, Japan, August 2017
2017	Impact of Sugar-Sweetened Beverages on Type 2 Diabetes Incidence in Ireland	Moderated Poster	European Association for the Study of Diabetes Annual Meeting, Lisbon, September 2017
2017	Health Service Utilisation and Related Costs Associated with Diabetes	Oral	SPHeRE Network Annual Conference, Dublin, January 2017
2017	Health Service Utilisation and Related Costs Associated with Diabetes	Rapid Fire	AUDGPI Annual meeting, Limerick, March 2017
2016	Urgent need for bariatric surgery in Ireland (acknowledgment for top presentation in session)	Moderated Poster	Society of Social Medicine, 60th Annual Scientific Meeting, York, September, 2016
2016	Health Service Utilisation and Related Costs Associated with Diabetes	Poster	National Health Service Research Institute Research Day, UCC, November, 2016
2016	Unmet Need for Bariatric Surgery	Oral	National Health Service Research Institute Research Day, UCC, November, 2016

Appendix 4 – Extra credit modules or other completed training

Year	Course
	Extra-credit modules, University College Cork
2018	PG7048 Generic and Transferable Skills Portfolio
2017	PG7016 Systematic Reviews for the health sciences
2016	PG7021 An Introduction to the Ethics of Health Research
	Other training completed during PhD
2018	Data Analysis in R – University College Cork
2017	Advanced Modelling Summer School – Leeds University, UK
2017	Cochrane Systematic Review Course - University College Cork
2016	Mediation analysis: challenges and novel approaches - University of Bristol, UK
2016	Masterclass in health economics and policy - NUI Galway
2016	NVIVO qualitative software training, UCC
2016	Symposium on Evidence Synthesis in Health Professions Education, UCC
2016	How to turbo charge your writing, UCC (Hugh Kearnes)
2016	Designing Effective Interventions for Health Behaviour Change, NUIG

Appendix 5 – Teaching contributions and student supervision

Academic Year	Module	Role
2017-2017	ST1001/ST1002 Introduction to Health Statistics	Tutor
2017-2018	EH2007 Health Information Systems II	Tutor
2017-2018	EH3012 Data Management	Tutor
2017-2018	BSc Public Health and Health Promotion	Mentor
2016-2017	ST1001/ST1002 Introduction to Health Statistics	Tutor
2016-2017	EH2007 Health Information Systems II	Tutor
2016-2017	EH3012 Data Management	Tutor
2016-2017	BSc Public Health and Health Promotion	Mentor
2105-2016	EH2007 Health Information Systems II	Tutor
2015-2016	BSc Public Health and Health Promotion	Mentor

Academic Year	Student	Project supervision
2017-2017	Niamh Bambury	MPH thesis: Trends in incidence of ischaemic stroke in people with and without diabetes in Ireland 2005-2015
2017-2018	Treasa Kelleher	MPH thesis: Modifiable predictors of incident depression in multimorbid older adults: results from The Irish Longitudinal Study on Ageing
2017-2018	Sarah Buggy	MPH thesis: Associations between maternal well-being and infant dietary intake at 18 months, in a low-income context
2016-2017	Grainne O'Sullivan	MPH thesis: Is childcare at 9 months and 3 years of age associated with weight status at 5 years of age in children in Ireland?
2016-2017	Aisling O'Brien	MPH thesis: prevalence of diabetes and its related microvascular and macrovascular complications in nationally representative, community dwelling older adults (aged ≥50) in Ireland, England and the United States of America (USA).
2016-2017	Aileen Callanan	HRB summer student: Evaluation of policy changes to the Dental Treatment Services Scheme (DTSS) and its impact on dental service use for older Irish adults with diabetes.

Appendix 6 – Published Papers

DOI: 10.1111/dme.13806

Research: Health Economics

Health service utilization and related costs attributable to diabetes

K. N. O'Neill[1], S. M. McHugh[1], M. L. Tracey[1], A. P. Fitzgerald[1,2] and P. M. Kearney[1]

[1]School of Public Health, University College Cork, Cork, Ireland and [2]Department of Statistics, University College Cork, Cork, Ireland

Accepted 23 August 2018

Abstract

Aims To estimate the health service use and direct healthcare costs attributable to diabetes using best available data and methods.

Methods A nationally representative sample of adults aged ≥50 years was analysed (n=8107). Health service use in the previous 12 months included the number of general practitioner visits, outpatient department visits, hospital admissions, and accident and emergency department attendances. Multivariable negative binomial regression was used to estimate the associations between diabetes and frequency of visits. Average marginal effects were applied to unit costs for each health service and extrapolated to the total population, calculating the incremental costs associated with diabetes.

Results The prevalence of diabetes was 8.0% (95% CI: 7.4, 8.6). In fully adjusted models, diabetes was associated with additional health service use. Compared to those without diabetes, people with diabetes have, on average, 1.49 (95% CI: 1.10, 1.88) additional general practitioner visits annually. Diabetes was associated with an 87% increase in outpatient visits, a 52% increase in hospital admissions and a 33% increase in accident and emergency department attendances (P<0.001). The incremental cost of this additional service use, nationally, is an estimated €88,894,421 annually, with hospital admissions accounting for 67% of these costs.

Conclusion Using robust methods, we identified substantially increased service use attributable to diabetes across the health system. Our findings highlight the urgent need to invest in the prevention and management of diabetes.

Diabet. Med. 35, 1727–1734 (2018)

Introduction

The number of people with diabetes has increased fourfold in the past 35 years and it is now the seventh leading cause of years lived with disability worldwide [1,2]. The impact of diabetes on health systems and national economies is of growing concern. In 2015, the global cost of diabetes was estimated to be US$1.31 trillion, with direct medical costs accounting for two-thirds of the costs [3]. Increasing prevalence combined with rising per capita medical expenditure indicate that the burden of diabetes on health systems will continue to escalate [4]. An understanding of the health service use and related costs associated with diabetes is necessary to inform national policies and the allocation of scarce resources. It is also essential for identifying and evaluating methods of cost saving.

Worldwide, there is a lack of accurate, comprehensive and comparable estimates of the health service use and costs attributable to diabetes [3]. This is largely due to the variation in methodologies employed [5]. Furthermore, the approach used affects the policy relevance of the estimates. There are three main methodological approaches: the sum-all medical approach; the disease-attributable approach; and incremental cost analysis. The most common method applied for estimating the cost of diabetes is the sum-all medical approach [5]. This method fails to identify service use attributable to diabetes and, thus, does not identify costs that can be avoided by diabetes prevention or management interventions. As a result, the sum-all medical approach does not provide meaningful estimates to inform policy decisions. Another common method used is the disease-attributable approach, whereby attributable fractions for conditions associated with diabetes are applied to health service use data to identify the proportion attributable to diabetes [5]. This method underestimates service use and the costs associated with diabetes because of its inability to capture use that does not appear directly attributable to diabetes [5,6]. For instance, mental health comorbidities in people

Correspondence to: Kate N. O'Neill. E-mail: kate.oneill@ucc.ie

What's new?

- Addressing many of the limitations of previous studies, our paper is one of the first European studies to quantify the excess health service use and costs independently attributable to diabetes.
- After accounting for important determinants of health service use, diabetes was associated with substantial additional health service use and costs across the health system. Hospital admissions account for two-thirds of the cost burden.
- We provide informative estimates for policy-makers, identifying the costs that can be directly targeted by diabetes prevention and management interventions and by highlighting areas for potential cost savings in the context of finite healthcare resources.

with diabetes increase health service utilisation [7]; however, because of its reliance on established quantifiable causal associations, disease-attributable methodology will not capture such excess service use.

More recent studies adopt an incremental costing approach. This method identifies the incremental health service use and costs for people with diabetes compared to those without, therefore capturing all costs associated with diabetes. The incremental costing approach also allows for the consideration of other factors known to influence health service use, including age, sex, ethnicity, education, socioeconomic status, health status and lifestyle factors [8]. Thus, it is possible to estimate health service use that is independently associated with diabetes [6,9]. To provide more precise estimates of the global cost of diabetes, there is an urgent need for valid and reliable country-level data [3]. This study aims to provide robust estimates of health service use and direct healthcare costs attributable to diabetes from a societal perspective by applying an incremental cost approach, with appropriate adjustment, using a nationally representative sample of a community-dwelling adults, aged ≥50 years, with and without diabetes.

Methods

Study design

A cross-sectional analysis of data from the first wave of The Irish Longitudinal Study of Ageing (TILDA) was conducted. TILDA is a nationally representative prospective cohort study of community-dwelling adults aged ≥50 years in the Republic of Ireland [10]. The sampling frame used for TILDA was the Irish Geodirectory, a comprehensive and up-to-date list of all residential addresses in Ireland. A multi-stage probability sampling design was used, with each residential address in the country having an equal probability of selection [10]. Eligible addresses were defined as any household with a person aged ≥50 years. All household residents aged ≥50 years were eligible to participate in the study. The estimated number of eligible households was 10 129. Of these, 6282 households participated (response rate 62%) and 8175 individuals were recruited. Ethical approval was obtained from the Trinity College Dublin Research Ethics Committee.

Data collection

Data collection occurred between October 2009 and November 2011. Participants were visited in their home by trained interviewers who used computer-assisted personal interviewing. This included detailed questions about sociodemographics, physical and mental health, self-reported doctor-diagnosis of chronic conditions and health service use.

Variable definition

The outcome of interest was self-reported health service use. Participants were asked about the frequency of visits to general practitioner (GP) services, outpatient department visits, hospital admissions and accident and emergency department (A&E) attendances in the past 12 months. They were also asked whether they had attended any of the following ancillary state services in the 12 months preceding the survey: dietitian; chiropody; optician; public health or community nurse; or psychology/counselling services. Individuals were classified as having diabetes if they self-reported a previous doctor diagnosis of diabetes. To distinguish between people with Type 1 and Type 2 diabetes, we defined those who were aged <50 years at diabetes diagnosis and reported injecting insulin, but who were not taking oral hypoglycaemic agents, as having Type 1 diabetes. All others were classified as having Type 2 diabetes. Participants who reported a doctor diagnosis of diabetes during the computer-assisted personal interviewing were asked the question, 'Has a doctor ever told you that you have any of the following conditions related to your diabetes?'. The conditions listed were: leg ulcer, protein in urine, lack of feeling and tingling pain in legs and feet due to nerve damage, damage to the back of the eye. Any participant who answered 'yes' to any of the above was considered to have a microvascular complication. Any participant who self-reported a doctor diagnosis of heart attack (myocardial infarction), heart failure (congestive cardiac failure), stroke (cerebrovascular accident) and mini stroke (transient ischaemic attack) was considered to have macrovascular complications. Other variables of interest included age (in years), gender, marital status (yes/no), education (primary, secondary, third level), location (urban/rural), healthcare cover (means tested public health insurance, private health insurance, both, neither), self-reported health status (excellent, very good, good, fair, poor) and other chronic conditions deemed not to be associated with diabetes.

These conditions were lung disease, asthma, arthritis, osteoporosis, cancer, Parkinson's disease and peptic ulcer disease.

Statistical analysis

Health service utilization was compared across populations with and without diabetes. The differences in the proportion of people attending each health service was analysed using Pearson's chi-squared test. An independent samples *t*-test was used to analyse the difference in the mean number of visits to each service. Logistic regression was used to model the association between diabetes and attendance at ancillary state services. Negative binomial regression models were used to analyse the association between diabetes and the frequency of health service use. Poisson, negative binomial, zero-inflated Poisson and zero-inflated negative binomial regression models were explored. Model selection was informed by Akaike Information Criterion and Bayesian Information Criterion statistics and by comparing predicted and observed probabilities, with negative binomial regression being selected as the most appropriate model (Appendix S1) [11]. Average marginal effects were calculated, providing an estimate of the excess number of visits/admissions attributable to diabetes on average. The average marginal effects were computed using the post-estimation command, *margins dydx*, in Stata. This calculates a predicted probability for each case with the fixed and observed values of variables, and then averages the predicted values [12].

The Anderson framework for the societal and individual determinants of healthcare utilization was used to inform the selection of appropriate variables to include in the multivariable regression models, with the aim of identifying the independent effect of diabetes on health service use [13]. The Anderson framework categorizes determinants as either predisposing, enabling or need factors. Any variables that could potentially mediate the association between diabetes and health service use were omitted. Multivariable regression was used to first adjust for predisposing factors (age, gender and marital status), then enabling factors (education, healthcare cover and location) and finally need factors (other chronic conditions).

Sampling weights were applied to all data analyses to adjust for differential non-response and to reduce the potential for participation or selection bias [10]. Complete data were available for 99.1% of the sample and so a complete case analysis was carried out. Analysis was carried out in Stata v.12 for windows (StataCorp, College Station, TX, USA) using the survey function (svy).

Calculation of costs

The average marginal effects for significant associations were applied to unit costs for the relevant health service. A societal perspective was adopted, applying average unit costs of €50 for a GP visit, €160 for an outpatient department visit, €5,030 for a hospital inpatient admission and €183 for an A&E attendance, previously calculated for Ireland [14,15]. These costs were extrapolated to the total population with diabetes to calculate the incremental health service costs. The total population with diabetes was estimated by applying the prevalence of diabetes in the sample to the most recent Irish census figures (2016). Cost estimates are reported in Euro and US dollars (USD) and were inflated to represent costs for 2016 using the Consumer Price Index (CPI) Inflation Calculator for Ireland [16]. To reflect uncertainty in the estimates of average unit costs, a sensitivity analysis was conducted whereby these estimates were varied by ± 20% [17].

Results

Of the 8107 participants included in the analysis, 51.9% were female and 41.5% were aged ≥65 years. The prevalence of diabetes was 8.0% (95% CI: 7.4, 8.6), only 11 participants had Type 1 diabetes. Among people with diabetes, 15.8% (95% CI: 13.0, 19.2) reported a macrovascular complication, while 26.3% (95% CI: 22.7, 30.3) reported a microvascular complication.

There were significant differences between the population with and without diabetes (Table 1). People with diabetes were older, included a lower proportion of women, lower levels of educational attainment and lower self-reported health status. They were also more likely to be covered by public health insurance. There was significantly higher service utilization among people with diabetes for all health services, except psychology/counselling services. Those with diabetes reported an average of 5.8 GP visits in the past 12 months compared with 3.8 visits among those without diabetes (P<0.001). Of people with diabetes, 60.8% (95% CI: 56.7, 64.8) reported attending an outpatient department in the last year compared with 39.1% (95% CI: 37.7, 40.5) of those without diabetes. A higher proportion of people with diabetes also reported being admitted to hospital in the previous 12 months [19.8% (95% CI: 16.7, 23.2)] than those without diabetes [12.4% (95% CI: 11.6, 13.2)]. Similar variations were observed for A&E attendances, with 20.5% (95% CI: 17.3, 24.1) of people with diabetes attending A&E compared with 14.9% (95% CI: 14.0, 15.8) of people without diabetes. When stratified by public health insurance coverage, similar patterns were observed (Appendix S2).

There were large statistically significant differences in the proportion of people attending all ancillary state services in the previous year between the two populations, other than attendance at a psychologist or counsellor (Table 1). The proportion of people with diabetes attending these services did not exceed 21%. Table 2 documents the adjusted odds ratios for attending ancillary state services for people with diabetes compared to those without. The odds of people with diabetes visiting a dietitian were 19.2 times those of people without diabetes (95% CI: 12.4, 29.6). People with diabetes were four times more likely to visit a chiropodist than those without (95% CI: 3.0, 5.5). Diabetes was also significantly associated

Table 1 Characteristics of population by diabetes diagnosis

	Population without diabetes (n=7486) %	Population with diabetes (n=621) %	P
Women	53	42	<0.001
Age			
50–64 years	60	44	
65–74 years	23	32	
≥75 years	17	25	<0.001
Rural residence	44	40	0.12
Married	66	63	0.11
Education			
None/primary	37	50	
Secondary	44	37	
Third level	19	13	<0.001
Healthcare cover			
Medical card	35	50	
Private health insurance only	38	25	
Dual cover	16	19	
No cover	11	7	<0.001
Diabetes-related condition			
Macrovascular	8	16	<0.001
Microvascular	-	26	
Other chronic illness*	47	51	0.07
Self-reported health			
Excellent/very good	55	33	
Good	30	32	
Fair/poor	15	36	<0.001
GP visits			
Attended past year	87	96	<0.001
Mean (SD) no. visits past year	3.8 (4.1)	5.8 (5.1)	<0.001
Outpatient department visits			
Attended past year	39	61	<0.001
Mean (SD) no. visits past year	1.1 (2.1)	2.2 (2.7)	<0.001
Hospital admissions			
Admitted in past year	12	20	<0.001
Mean (SD) no. admissions past year	0.2 (0.6)	0.3 (.08)	<0.001
A&E attendance			
Attended in past year	15	21	<0.001
Mean (SD) no. visits past year	0.2 (0.7)	0.3 (0.8)	0.01
Access to ancillary state service			
Dietitian	0.6	11	<0.001
Chiropody services	4	16	<0.001
Optician	12	21	<0.001
Public health/community nurse	6	12	<0.001
Psychology/counselling services	0.8	1.2	0.40

A&E, accident and emergency department; GP, general practitioner; SD, standard deviation.
*Lung disease, asthma, arthritis, osteoporosis, cancer, Parkinson's disease and peptic ulcer disease.

with ~60% increased odds of attendance at an optician or public health nurse, with odds ratios of 1.58 (95% CI: 1.27, 1.96) and 1.57 (95% CI: 1.17, 2.10), respectively.

The incidence rate ratios (IRRs) and average marginal effects from the multivariable negative binomial regression models are presented in Table 3. There were statistically significant positive associations between diabetes and the frequency of GP visits, outpatient department visits, hospital admissions and A&E attendances. Adjustment for important confounding variables resulted in an attenuation of the IRR point estimates. In the fully adjusted models, people with diabetes had a higher rate of GP visits, with an IRR of 1.39 (95% CI: 1.29, 1.50). A similar pattern was observed for outpatient department visits and hospital admissions. Diabetes was associated with an 87% increase in outpatient department visits and a 52% increase in hospital admissions (P<0.001). A&E attendance was also associated with diabetes (IRR 1.33; 95% CI: 1.06, 1.66). On average, 1.49 (95% CI: 1.10, 1.88) additional GP visits were attributable to diabetes in a 12-month period and approximately one additional outpatient visit [0.97 (95% CI: 0.73, 1.21)].

Table 2 Adjusted odds ratios for the association between diabetes diagnosis and ancillary service use in previous 12-month period

Ancillary service	Adjusted odds ratio (95% CI)*	P
Dietitian	19.2 (12.4, 29.6)	<0.001
Chiropody	4.06 (3.00, 5.50)	<0.001
Optician	1.58 (1.27, 1.96)	<0.001
Public health/community nurse	1.57 (1.17, 2.10)	0.003
Psychology/counselling service	1.47 (0.66, 3.27)	0.34

*Models adjusted for age, gender, marital status, urban/rural location, education, healthcare cover, chronic conditions.

The population-based cost estimates for the incremental health service use associated with diabetes are shown in Table 4. The total population in Ireland in 2016 aged ≥50 years was 1 446 460. The prevalence of diabetes in this sample was applied, estimating that 115 717 adults aged ≥50 years had diabetes in Ireland. The incremental health service use associated with diabetes was estimated to cost €88,894,421 per annum. Hospital admissions accounted for the majority of this spending, costing an estimated €60,002,517. The results of the sensitivity analysis are shown in Table 5. By varying the unit cost estimates by ± 20%, the cost of the incremental health service use associated with diabetes fluctuated from €71,115,537 to €106,673,305.

Discussion

Using a large nationally representative population-based study, we provide robust estimates of health service use and related costs attributable to diabetes. We identify substantial increased service use associated with diabetes across the health system. Due to the high costs of hospital admissions, hospitalization costs place the largest burden on the health service, accounting for more than two-thirds of the total costs attributable to diabetes.

Diabetes was associated with a 39% increase in GP visits and an 87% increase in outpatient department visits. This translated to an additional 1.49 GP visits on average per

Table 3 Multivariable negative binomial regression results

Health service	Model 1: Crude IRR (95% CI)	Model 1: Crude AME (95% CI)	Model 2: Predisposing IRR (95% CI)	Model 2: Predisposing AME (95% CI)	Model 3: Enabling IRR (95% CI)	Model 3: Enabling AME (95% CI)	Model 4: Need IRR (95% CI)	Model 4: Need AME (95% CI)
GP visits	1.53 (1.42, 1.64) *P*<0.001	1.99 (1.58, 2.40) *P*<0.001	1.50 (1.38, 1.62) *P*<0.001	1.88 (1.45, 2.32) *P*<0.001	1.38 (1.28, 1.49) *P*<0.001	1.46 (1.08, 1.84) *P*<0.001	1.39 (1.29, 1.50) *P*<0.001	1.49 (1.10, 1.88) *P*<0.001
Outpatient department	1.93 (1.73, 2.17) *P*<0.001	1.04 (0.81, 1.27) *P*<0.001	1.91 (1.70, 2.14) *P*<0.001	1.01 (0.79, 1.24) *P*<0.001	1.77 (1.58, 1.99) *P*<0.001	0.87 (0.65, 1.08) *P*<0.001	1.87 (1.65, 2.11) *P*<0.001	0.97 (0.73, 1.21) *P*<0.001
Hospital admission	1.68 (1.35, 2.09) *P*<0.001	0.12 (0.06, 0.19) *P*<0.001	1.58 (1.26, 1.98) *P*<0.001	0.11 (0.04, 0.17) *P*=0.001	1.49 (1.20, 1.85) *P*<0.001	0.09 (0.03, 0.15) *P*=0.002	1.52 (1.21, 1.91) *P*<0.001	0.10 (0.03, 0.16) *P*=0.002
A&E attendance	1.42 (1.15, 1.77) *P*=0.001	0.09 (0.03, 0.16) *P*=0.006	1.41 (1.13, 1.77) *P*=0.002	0.09 (0.02, 0.16) *P*=0.008	1.34 (1.07, 1.68) *P*=0.01	0.08 (0.01, 0.14) *P*=0.02	1.33 (1.06, 1.66) *P*=0.01	0.07 (0.01, 0.14) *P*=0.03

A&E, accident and emergency department; AME, average marginal effect; GP, general practitioner; IRR, incidence rate ratio.
Model 1: crude association; Model 2: adjusted for age, gender, marital status; Model 3: adjusted for age, gender, marital status, education, healthcare cover, location; Model 4: adjusted for age, gender, marital status, education, healthcare cover, location, chronic conditions.

annum and approximately one additional outpatient visit. Because of the higher unit cost of outpatient visits, the associated costs were more than twice those of primary care costs. With ageing populations and the increasing burden of chronic disease, greater attention has been paid to coordinating patient care according to levels of disease complexity. There has been a shift towards multidisciplinary shared management of complex cases of diabetes across primary and secondary care settings, and structured management of people with uncomplicated diabetes in primary care with suitable organizational support [18]. The present findings suggest this shift in routine care settings could result in considerable cost savings.

Diabetes diagnosis was associated with increased hospital admissions, in line with a number of international studies that document higher rates of hospitalizations in people with diabetes [19,20]. While many studies only take age and gender into consideration, our findings add to the literature by indicating that, in a population-based sample, diabetes remains associated with a higher number of hospital admissions after controlling for a wide range of important potential confounders. Our analysis shows that diabetes was associated with a 52% higher number of admissions. Because of variations in study populations and methodological approaches, direct comparisons with previous studies are limited. One study conducted in Tayside, Scotland, reported a 100% higher rate of hospital admissions in people with diabetes compared to those without [21]. This was a crude estimate and the study population was significantly younger.

Almost 70% of the health service costs associated with diabetes resulted from hospital admissions. Numerous studies report hospital admissions as the main driver of costs associated with diabetes and our findings highlight the need to provide effective interventions for the management of diabetes and related complications [22,23]. Increased risk of hospitalization in people with diabetes is attributable to macrovascular and microvascular complications [19,24]. While significantly higher than the population without diabetes, it is concerning that less than one-quarter of people with diabetes reported attending ancillary state services, such as chiropody and dietetic services. A shortage of allied health professionals has previously been identified as a barrier to delivering diabetes care in Ireland [25]. International guidelines identify these services as part of routine care for people with diabetes [26]. Such services, specifically foot care services and dietetic interventions for people with diabetes, are effective in preventing complications and subsequently reducing healthcare expenditure [27]. While these services may be available privately, at a significant cost to the patient, it is imperative that such effective services are accessible to all people with diabetes.

Addressing many of the limitations of previous studies, we provide robust estimates of health service utilization attributable to diabetes. By adopting an incremental approach, we ensured that any excess health service use attributable to

Table 4 Total incremental health service costs attributable to diabetes

Health service	Direct costs (95% CI) Euro	USD
GP visits	8,886,425 (6,560,448–11,212,403)	10,358,107 (7,645,924–13,069,288)
Outpatient department visits	18,512,617 (13,932,175–23,093,058)	21,578,491 (16,239,483–26,917,499)
Hospital admissions	60,002,517 (18,000,755–96,004,027)	69,939,533 (20,981,860–111,903,253)
A&E attendances	1,492,862 (213,266–2,985,725)	1,740,095 (248,585–3,480,191)
Total	88,894,421 (38,706,645–133,295,212)	103,616,226 (45,116,852–155,370,232)

A&E, accident and emergency department; GP, general practitioner; USD, US dollars.

Table 5 Sensitivity analysis: total incremental health service costs attributable to diabetes

Health service	Direct costs, € (95% CI) –20%	+20%
GP visits	7,109,140 (5,248,359, 8,969,922)	10,663,710 (7,872,538, 13,454,883)
Outpatient department visits	14,810,093 (11,145,740, 18,474,446)	22,215,140 (16,718,612, 27,711,669)
Hospital admissions	48,002,013 (14,400,604, 76,803,221)	72,003,020 (21,600,906, 115,204,832)
A&E attendances	1,194,290 (170,613, 2,388,580)	1,791,435 (255,919, 3,582,870)
Total	71,115,537 (30,965,316, 106,636,169)	106,673,305 (46,447,974, 159,954,254)

A&E, accident and emergency department; GP, general practitioner.

diabetes was identified, not just the service use that appeared directly related to diabetes. For instance, this approach ensured that excess service use associated with mental health issues was captured in our results. A nationally representative sample provides an appropriate comparison group to calculate incremental use and costs, avoiding the overrepresentation of people with diabetes and diabetes-related complications. To date, studies have largely relied on hospital-based samples or administrative healthcare data [5]. Unlike much of the existing literature on the cost of diabetes, we specifically address the issue of endogeneity [5]. The present study accounts for important confounding variables that have previously been recognized as predictors of service use, identifying the costs that can be independently attributed to diabetes [8]. The adjustment for such factors led to the attenuation of our estimates. Most incremental studies control for gender and age only, because of data availability constraints [3,5,24,28], and so may overestimate service use and costs attributable to diabetes. Furthermore, any variables identified as potential mediating factors were omitted from the analyses ensuring that the findings were not an underestimation of the true association between diabetes and health service use. To date, the only nationally representative studies adopting the incremental costing approach and adjusting for additional factors were conducted in the USA [4,9].

While we cannot infer causality because of the cross-sectional nature of the data, almost 90% of the cohort had attended the GP in the previous year. Thus, the potential for reverse causality whereby those who attend the GP are more likely to be diagnosed with diabetes and diabetes-related complications is reduced. Furthermore, <1% of the cohort had undiagnosed diabetes on the basis of HbA_{1c} measurement [29]. While the reliance on self-report doctor diagnoses may potentially introduce misclassification bias and result in inaccurate estimates, evidence shows that self-report is a suitable measure for estimating the prevalence of chronic conditions including diabetes when compared to medical records [30]. Health service utilization is also based on self-report, introducing potential for measurement bias. However, recent studies suggest there is no evidence of differential recall bias according to demographics or health status [31]. This method is widely used in health services research. The data were weighted to adjust for differential non-response with the aim of minimizing the potential for selection bias and improving the representativeness of the findings; however, our estimates are only representative of the excess health service use and costs associated with diabetes in community-dwelling adults aged ≥50 years and so do not represent costs for the total population. It is estimated that <1.6% of the adult population aged ≥50 years in Ireland are in long-term residential care [32]. It is also important to note that cost estimates are based on average unit costs per visit/admission. Diabetes-related admissions are more expensive and as a result our cost estimates are likely to be an underestimation of the true costs of hospital admissions [22].

The cost estimates also only refer to additional service use for GP and hospital services. As a result of data limitations, we were unable to calculate the costs associated with ancillary service use or community care. Although we took a societal perspective in calculating the associated costs, our estimates represent the direct medical costs and do not consider the indirect costs associated with excess health service use. The accuracy of our estimates could be improved in further research by applying the demonstrated methods to individual-level cost data. The challenge, however, is to find a data source with all the necessary information. In the absence of a unique identifier in Ireland, this was not possible.

In conclusion, our findings show that diabetes is associated with substantial additional health service use and costs, with hospital admissions accounting for more than two-thirds of the cost burden. We highlight areas for potential cost savings in the context of finite healthcare resources, such as a shift in routine management to primary care and improved access to effective ancillary services, such as foot care services and dietetic interventions [27]. We provide robust informative estimates for policy-makers by identifying additional health service use and costs that are attributable to diabetes. Effective interventions aimed specifically at both diabetes prevention and management therefore have the potential to have a direct impact on these healthcare costs. The challenge is to identify cost-effective interventions, examine the trade-offs between them, and determine how best to implement them.

Funding sources

K.O'N. and P.K. are funded by the Health Research Board Research Leader Award (RL/2013/7).

Competing interests

None declared.

Acknowledgements

We acknowledge all TILDA participants. TILDA was supported by Department of Health and Children, the Atlantic Philanthropies and Irish Life. We wish to acknowledge the staff and researchers at the TILDA centre in Trinity College Dublin and the Irish Social Science Data Archive (ISSDA) for providing access to the data.

References

1 Zhou B, Lu Y, Hajifathalian K, Bentham J, Di Cesare M, Danaei G *et al*. Worldwide trends in diabetes since 1980: A pooled analysis of 751 population-based studies with 4.4 million participants. *Lancet* 2016; **387**: 1513–1530.
2 Vos T, Barber RM, Bell B, Bertozzi-Villa A, Biryukov S, Bolliger I *et al*. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: A systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015; **386**: 743–800.
3 Bommer C, Heesemann E, Sagalova V, Manne-Goehler J, Atun R, Bärnighausen T *et al*. The global economic burden of diabetes in adults aged 20–79 years: a cost-of-illness study. *Lancet Diabetes Endocrinol* 2017; **3633**: 423–430.
4 Zhuo X, Zhang P, Kahn HS, Bardenheier BH, Li R, Gregg EW. Change in medical spending attributable to diabetes: National data from 1987 to 2011. *Diabetes Care* 2015; **38**: 581–587.
5 Seuring T, Archangelidi O, Suhrcke M, Seuring T, Suhrcke ÁM, Archangelidi O *et al*. The Economic Costs of Type 2 Diabetes: A Global Systematic Review. *Pharmacoeconomics* 2015; **33**: 811–831.
6 Honeycutt AA, Segel JE, Hoerger TJ, Finkelstein EA. Comparing cost-of-illness estimates from alternative approaches: An application to diabetes. *Health Serv Res* 2009; **44**: 303–320.
7 Calderón-Larrañaga A, Abad-Díez JM, Gimeno-Feliu LA, Marta-Moreno J, González-Rubio F, Clerencia-Sierra M *et al*. Global health care use by patients with type-2 diabetes: Does the type of comorbidity matter? *Eur J Intern Med* 2015; **26**: 203–210.
8 Hudson E, Nolan A. Public healthcare eligibility and the utilisation of GP services by older people in Ireland. *J Econ Ageing* 2015; **6**: 24–43.
9 Trogdon JG, Hylands T. Nationally representative medical costs of diabetes by time since diagnosis. *Diabetes Care* 2008; **31**: 2307–2311.
10 Whelan BJ, Savva GM. Design and methodology of the Irish Longitudinal Study on Ageing. *J Am Geriatr Soc* 2013; **61**: 265–268.
11 Long S, Freese J. *Regression Models for Categorical Dependent Variables Using Stata, Revised Edition. 3rd ed*. College Station, TX: Stata Press, 2014.
12 Williams R. Using the margins command to estimate and interpret adjusted predictions and marginal effects. *Stata J* 2012; **12**: 308–331.
13 Andersen R, Newman JF. Societal and individual determinants of medical care utilisation in the United States. *Milbank Mem Fund Q* 1973; **51**: 95–124.
14 Comptroller and Auditor General. Health Service Executive Emergency Departments 2009. Available at http://audgen.gov.ie/documents/vfmreports/70_Emergency_Departments.pdf. Last accessed 01 June 2018.
15 Glynn LG, Valderas JM, Healy P, Burke E, Newell J, Gillespie P *et al*. The prevalence of multimorbidity in primary care and its effect on health care utilization and cost. *Fam Pract* 2011; **28**: 516–523.
16 Central Statistics Office. *Consumer Price Index Inflation Calculator for Ireland*. Dublin: Central Statistics Office [Cited 2018 July 26]. Available at https://www.cso.ie/en/interactivezone/visualisationtools/cpiinflationcalculator/. Last accessed 26 July 2018.
17 Health Information and Quality Authority. *Health technology assessment of human papillomavirus testing as the primary screening method for prevention of cervical cancer*. Dublin: Health Information and Quality Authority, 2017.
18 Kahn R, Anderson JE. Improving diabetes care: The model for health care reform. *Diabetes Care* 2009; **32**: 1115–1118.
19 De Berardis G, D'Ettorre A, Graziano G, Lucisano G, Pellegrini F, Cammarota S *et al*. The burden of hospitalization related to diabetes mellitus: A population-based study. *Nutr Metab Cardiovasc Dis* 2012; **22**: 605–612.
20 Bo S, Ciccone G, Grassi G, Gancia R, Rosato R, Merletti F *et al*. Patients with type 2 diabetes had higher rates of hospitalization than the general population. *J Clin Epidemiol* 2004; **57**: 1196–1201.
21 Donnan P, Leese G, Morris A. Hospitalizations for People With Type 1 and Type 2 Diabetes Compared With the Nondiabetic

Population of Tayside. *Scotland*. *Diabetes Care* 2000; **23**: 1774–1779.
22 Yang W, Dall TM, Halder P, Gallo P, Kowal SL, Hogan PF *et al*. Economic costs of diabetes in the U.S. in 2012. *Diabetes Care* 2013; **36**: 1033–1046.
23 Ozieh MN, Bishu KG, Dismuke CE, Egede LE. Trends in health care expenditure in U.S. adults with Diabetes: 2002-2011. *Diabetes Care* 2015; **38**: 1844–1851.
24 Bruno G, Picariello R, Petrelli A, Panero F, Costa G, Cavallo-Perin P *et al*. Direct costs in diabetic and non diabetic people: The population-based Turin study. *Italy*. *Nutr Metab Cardiovasc Dis* 2012; **22**: 684–90.
25 Riordan F, McHugh SM, Murphy K, Barrett J, Kearney PM. The role of nurse specialists in the delivery of integrated diabetes care: a cross-sectional survey of diabetes nurse specialist services. *BMJ Open* 2017; **7**: e015049.
26 American Diabetes Association (ADA). Standard of medical care in diabetes - 2017. *Diabetes Care* 2017; **40**: s4–128.
27 Li R, Zhang P, Barker LE, Chowdhury FM, Zhang X. Cost-effectiveness of interventions to prevent and control diabetes mellitus: A systematic review. *Diabetes Care* 2010; **33**: 1872–94.
28 Köster I, Von Ferber L, Ihle P, Schubert I, Hauner H. The cost burden of diabetes mellitus: The evidence from Germany - The CoDiM study. *Diabetologia* 2006; **49**: 1498–1504.
29 Leahy S, O' Halloran AM, O' Leary N, Healy M, McCormack M, Kenny RA *et al*. Prevalence and correlates of diagnosed and undiagnosed type 2 diabetes mellitus and pre-diabetes in older adults: Findings from the Irish Longitudinal Study on Ageing (TILDA). *Diabetes Res Clin Pract* 2015; **110**: 241–249.
30 Okura Y, Urban LH, Mahoney DW, Jacobsen SJ, Rodeheffer RJ. Agreement between self-report questionnaires and medical record data was substantial for diabetes, hypertension, myocardial infarction and stroke but not for heart failure. *J Clin Epidemiol* 2004; **57**: 1096–1103.
31 Reijneveld SA, Stronks K. The validity of self-reported use of health care across socioeconomic strata: a comparison of survey and registration data. *Int J Epidemiol* 2001; **30**: 1407–1414.
32 Information Unit, Department of Health. *Long-Stay Activity Statistics 2011*. Dublin: Department of Health, 2011.

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Appendix S1. Model diagnostics for the multivariable model.
Appendix S2. Health service utilization and socio-economic status.

ELSEVIER

CrossMark

Surgery for Obesity and Related Diseases 13 (2017) 1052–1056

SURGERY FOR OBESITY AND RELATED DISEASES

Original article

Unmet need for bariatric surgery

Kate N. O'Neill, M.Phil.[a,*], Francis M. Finucane, M.D., F.R.C.P.I.[b], Carel W. le Roux, M.B.Ch.B., Ph.D.[c], Anthony P. Fitzgerald, Ph.D.[a,d], Patricia M. Kearney, F.R.C.P.I., Ph.D.[a]

[a]Department of Epidemiology and Public Health, University College Cork, Ireland
[b]Bariatric Medicine Service, Galway Diabetes Research Centre, HRB Clinical Research Facility, Galway, Ireland
[c]Diabetes Complications Research Centre, Conway Institute, University College Dublin, Ireland
[d]Department of Statistics, University College Cork, Ireland

Received December 15, 2016; accepted December 16, 2016

Abstract

Introduction: With the rising prevalence of severe obesity and type 2 diabetes (T2D), bariatric surgery offers a clinical and cost-effective treatment for carefully selected patients. Despite this, the provision of surgical services varies significantly between countries.

Objective: To inform health service planning by estimating the number of people who would potentially benefit from bariatric surgery.

Setting: Nationally representative sample of community-dwelling older adults.

Methods: We applied two separate evidence-based criteria sets for eligibility for bariatric surgery. For the first set of criteria, we considered those with body mass index $\geq$40 kg/m^2 or $\geq$35 kg/m^2 and one or more of the following: T2D, hypertension, previous myocardial infarction, or sleep apnea. For the second set of criteria, we considered patients with T2D and body mass index $\geq$35 kg/m^2, with one or more of the following: previous myocardial infarction, elevated urine albumin-creatinine ratio, retinopathy, neuropathy, or peripheral vascular disease. Prevalence estimates were applied to census figures for 2011, estimating absolute numbers meeting the criteria.

Results: Among adults aged $\geq$50 years, 7.97% (95% confidence interval [CI]: 7.23, 8.78), representing 92,573 people (95% CI: 83,978, 101,981), met criteria one and 0.97% (95% CI: 0.73, 1.28), representing 11,231 people (95% CI: 8471, 14,890), met criteria two. With fewer than 1/100,000 population publicly funded surgeries taking place annually, current service provision meets much less than 0.1% of the need.

Conclusions: While many adults who fulfill the eligibility criteria for bariatric surgery may not want or require it, the current level of need for bariatric surgical services is not being met. A strategy to develop and expand the provision of bariatric care is urgently needed. (Surg Obes Relat Dis 2017;13:1052–1056.)

Keywords: Bariatric surgery eligibility; Severe obesity; Type 2 diabetes

With the prevalence of severe obesity and type 2 diabetes (T2D) continuing to rise [1–4], the increasing evidence on the clinical and cost-effectiveness of bariatric surgery makes it an attractive treatment option [5,6]. A Cochrane review investigating the effect of bariatric surgery for overweight and obese patients found surgery to be more clinically effective in the treatment of severe obesity than other nonsurgical interventions [7]. While most trials only follow participants for up to 3 years [8], data from observational studies with 10- to 20-year follow-up show the benefits of surgery [7,9]. The Swedish Obese Patients prospective case-control study demonstrates the benefits of bariatric surgery in maintaining weight loss for 20 years [10]. Compared

*Correspondence: Kate O'Neill, University College Cork, Department of Epidemiology and Public Health, Western Gateway Building, Cork, Ireland.

E-mail: kate.oneill@ucc.ie

http://dx.doi.org/10.1016/j.soard.2016.12.015
1550-7289/

with usual care, bariatric surgery is also associated with a long-term reduction in overall morbidity and mortality [10,11]. The largest benefit of bariatric surgery is observed among people with T2D [11], with international diabetes organizations now calling for the inclusion of metabolic surgery among antidiabetes interventions for people with T2D and obesity [6]. Substantially higher diabetes remission rates are observed among people with T2D after bariatric surgery (adjusted odds ratios for remission after 2 years was 8.42 ($P < .001$) and 3.45 ($P < .001$) after 10 years) [10]. In the UK national registry of bariatric surgical patients, 65% of patients with diabetes achieved good glycemic control after surgery, returning to a state of no indication of diabetes without medication [12]. This represents a large reduction in direct healthcare costs associated with diabetes. The cost-effectiveness of bariatric surgery is most notable in patients with high direct healthcare costs secondary to the complications of obesity, such as diabetes [9]. A UK health technology assessment found that for patients with diabetes and a body mass index (BMI) of 30–39 kg/m^2 the incremental-cost-effective-ratio was £1367 ($1684) per quality-adjusted life-year gained [13]. For patients with T2D (ranging from newly diagnosed to those requiring multimodal therapies), the costs of surgery will be recuperated within 3 years [10,14]. This can potentially be further improved in the subgroup of patients with T2D with the highest direct healthcare costs, such as those requiring expensive insulin or GLP-1 analogues or the subgroup of patients with established complications of diabetes such as micro- and macrovascular disease [15].

Despite the global obesity and diabetes epidemics and the demonstrated clinical and cost-effectiveness of bariatric surgery, there is large variation in service provision between countries. The rate of bariatric surgery in North America is 44 per 100,000 people, while Sweden performs 78 surgeries per 100,000 people. In comparison, the rate of surgery is <10 per 100,000 in the UK or Germany [16]. Periodic assessment of bariatric surgery rates is an important source of knowledge to healthcare providers and governments [17]. Furthermore, to inform health policy and resource allocation, an estimate of the prevalence of eligibility for bariatric surgery would be helpful. Bariatric surgical procedures are not commonly performed in Ireland. There is currently no national registry of bariatric surgical patients, so robust information about how many procedures are done is limited. However, only two public bariatric centers exist nationally and between them fewer than 50 procedures are done per annum, equivalent to less than 1 publicly funded surgery taking place annually per 100,000 people. Ireland has a two-tier health system, whereby all citizens are entitled to healthcare under the public system, funded mainly through general taxation. Private health insurance acts as duplicate cover, providing faster access to care [18]. While an unknown number of bariatric surgeries are carried out in the private sector, this provision is dependent on individuals' ability to pay.

Ireland has one of the highest rates of obesity in Europe, with 1 in 4 adults estimated to suffer with obesity [18]. The prevalence of doctor diagnosed diabetes has increased from 2.2% of the adult population in 1998 to 5.2% in 2015 [19]. The prevalence of T2D among adults aged over 50 years in Ireland is 8.5% [20]. We sought to estimate the number of people potentially eligible for bariatric surgery in Ireland based on established clinical criteria and then to refine the number of potentially eligible patients by identifying those who suffer from the diseases with high morbidity, mortality, and healthcare cost, that respond best to bariatric surgery.

Methods

We applied two separate sets of criteria to identify those potentially eligible for bariatric surgery. The first set of criteria, based on UK guidelines [9], included a BMI ≥ 40 kg/m^2 or a BMI ≥ 35 kg/m^2 and one or more of the following conditions: T2D, hypertension, previous myocardial infarction (MI), and sleep apnea. The second set of criteria applied only to those patients with T2D and BMI ≥ 35 kg/m^2, who had one or more of the following conditions; previous MI, elevated urine albumin-creatinine ratio, retinopathy, neuropathy, or peripheral vascular disease. This second set of criteria was used to identify the cohort of patients in whom the largest benefits and cost-savings from bariatric surgery are observed [13,15].

We conducted a cross sectional analysis of the first wave (2009–2011) of The Irish Longitudinal Study on Ageing (TILDA) to estimate the proportion of people eligible for bariatric surgery. TILDA is a nationally representative cohort study of community-dwelling adults aged 50 years and over. The sampling frame is the Irish Geodirectory, which is a comprehensive and up-to-date list of all residential addresses in Ireland. A multistage probability sampling design was used, with each residential address in the country having an equal probability of selection. All household residents aged ≥ 50 years were eligible to participate in the study. Participants completed a computer-assisted personal interview (CAPI) administered by trained social interviewers which included questions on self-reporting doctor diagnosis of chronic conditions. Those who completed the CAPI were invited to attend a health assessment either at the study center or in their home [21]. During the health assessment, trained nurses objectively measured participants' weight and height. These measures were used to calculate BMI. Only those who completed the health assessment are included in the analysis.

Individuals were classified as having diabetes if they self-reported a previous doctor diagnosis. Type 1 diabetes was defined as those who were aged less than 50 years at diabetes diagnosis and reported injecting insulin, but not taking oral hypoglycemic agents. All others were classified as having T2D. Participants were asked "Has a doctor ever told you that you have any of the conditions on this card?", which included high blood pressure and heart attack (including MI or coronary thrombosis). Those who responded "yes" were considered to have the named condition. Participants were asked "How likely are you to doze off or fall asleep during the day?" with four different response options: 0 = would never doze; 1 = slight chance of dozing; 2 = moderate chance of dozing; and 3 = high chance of dozing. This question was considered a surrogate for the Epworth Sleepiness Scale [22]. For the purpose of this analysis, those who responded with "high chance of dozing" were classified as having sleep apnea. Participants who reported a doctor diagnosis of diabetes during the CAPI were asked the question "Has a doctor ever told you that you have any of the following conditions related to your diabetes?" The conditions listed were: leg ulcer, protein in urine, lack of feeling and tingling pain in legs and feet due to nerve damage, or damage to the back of your eye. Those who responded "yes" were considered to have peripheral vascular disease, elevated urine albumin-creatinine ratio, diabetic neuropathy, or diabetic retinopathy, respectively.

Survey weights were applied to the analysis to reflect the complex sampling design and to adjust for participation bias. Based on comparisons with the Irish census and the 2010 Quarterly National Household Survey, a weight was constructed adjusting for differences in educational attainment, age, sex, marital status, and geographic location. The survey weights applied also accounted for nonresponse bias in the health assessment sample, as previously described [23]. The number of participants meeting the eligibility criteria for the two sets of criteria was calculated and expressed as a percentage with corresponding 95% confidence intervals (CIs), using Poisson regression. Prevalence estimates were applied to the most recent Irish census figures (2011) to determine absolute numbers meeting these criteria. Based on evidence from the UK national registry of bariatric surgical patients, a diabetes remission rate of 65% was applied to model the number of people with T2D and microvascular complications (criteria two) with potential remission of diabetes following surgery [12]. Due to the crude measure used for sleep apnea, a sensitivity analysis was conducted excluding those who were defined as eligible for surgery based solely on having sleep apnea. Analysis was carried out in Stata v.12 for windows (StataCorp, College Station, TX, USA) using the survey function (svy).

Results

A total of 8,175 participants from 6,282 households completed the CAPI (response rate: 62%). Of these, 5,873 (71%) participants completed the health assessment and were included in the analysis. The cohort comprised 51.7% females and the mean age was 62.9 years. Of the participants, 21.2% (95% CI: 20.1, 22.4) had a normal BMI and 42.7% (95% CI: 41.4, 44.1) had a BMI between 25 kg/m^2 and 29.9 kg/m^2. In assessing obesity, 25.2% (95% CI: 24.1, 26.4) of the population had moderate obesity while 7.7% (95% CI: 7.0, 8.5) and 2.7% (95% CI: 2.3, 3.1) had severe and morbid obesity, respectively. The prevalence of T2D was 7.74% (95% CI: 7.08, 8.45) and the prevalence of doctor diagnosed hypertension was 37.9% (95% CI: 36.5, 39.3).

Under criteria one, 444 participants were eligible for bariatric surgery (patients with a BMI $\geq$40 or $\geq$35 kg/m^2 and one or more of the following conditions: T2D, hypertension, previous MI, or sleep apnea). This accounted for 7.97% (95% CI: 7.23, 8.78) of the population (Table 1). In the sensitivity analysis excluding those eligible for surgery based solely on having sleep apnea, this reduced to 7.42% (95% CI: 6.72, 8.19). There were 112 (2.06%; 95% CI: 1.70, 2.49) participants with a BMI $\geq$35 kg/m^2 and T2D. Under the second set of criteria, 50 participants were eligible for bariatric surgery (patients with a BMI $\geq$35 kg/m^2, T2D, and one or more of the following complications: previous MI, elevated urine albumin creatinine ratio, retinopathy, neuropathy, and peripheral vascular disease). This accounted for 0.97% (95% CI: 0.73, 1.28) of the population (Table 2).

The total proportion of people eligible for bariatric surgery under the two sets of criteria were applied to the 2011 Irish census figures to estimate the absolute numbers with potential indication for bariatric surgery in Ireland. The total population aged $\geq$50 years was 1,161,512. The total number of people with potential indication for bariatric surgery under the first set of criteria, was 92,573 (95% CI: 83,978, 101,981). Under the second set of criteria, 11,231 (95% CI: 8471, 14,890) people were eligible for bariatric surgery.

The UK national registry of bariatric surgical patients with diabetes, operated on between 2011 and 2013, shows 65% had acceptable glycemic control without medication after surgery [12]. By applying these results to Irish patients

Table 1
Distribution of clinical conditions among TILDA participants for criteria one

Condition	n	% (95% CI)	Population Estimate n (95% CI)
BMI $\geq$40 kg/m^2	145	2.66 (2.25, 3.13)	
BMI $\geq$35 kg/m^2 and:			
Type 2 diabetes	112	2.06 (1.70, 2.49)	
Hypertension	336	6.08 (5.43, 6.79)	
Previous MI	37	0.67 (0.48, 0.94)	
Sleep apnea	119	2.19 (1.81, 2.65)	
Any*	444	7.97 (7.23, 8.78)	92,573 (83,978, 101,981)

BMI = body mass index; MI = myocardial infarction; TILDA = The Irish LongituDinal study of Aging.
*Categories of participants are not mutually exclusive.

Table 2
Distribution of complications among TILDA participants with BMI $\geq$35 kg/m^2 and type 2 diabetes (criteria 2)

Condition	n	% (95% CI)	Population Estimate n (95% CI)
Previous MI	15	0.29 (0.17, 0.50)	
Protein in urine	14	0.25 (0.15, 0.41)	
Retinopathy	17	0.36 (0.22, 0.58)	
Neuropathy	21	0.39 (0.25, 0.60)	
Peripheral vascular disease	10	0.19 (0.10, 0.35)	
Any*	50	0.97 (0.73,1.28)	11,231 (8,471, 14,890)

BMI = body mass index; MI = myocardial infarction; TILDA = The Irish LongituDinal study of Aging.
*Categories of participants are not mutually exclusive.

with complicated T2D (criteria two), we estimated that prioritizing bariatric surgery for this cohort could result in an estimated 7,301 patients achieving good glycemic control, without requiring medication for up to two years after surgery.

Discussion

It is evident that a substantial proportion of older Irish adults are potentially eligible for bariatric surgery. While many adults who fulfill the criteria may not want or be suitable for bariatric surgery, these findings highlight the high level of need for such services in Ireland. With an estimate of less than 1 publicly funded surgery taking place annually per 100,000 people, our findings indicate that current public service provision of bariatric surgery in Ireland meets much less than 0.1% of the need. This mirrors the situation in other countries, such as the UK, where it is estimated that 2.5 million people are eligible for surgery with less than 10,000 surgeries occurring annually [9].

Obesity poses a major challenge for public health. Public health strategies focus on the prevention of obesity and lifestyle interventions. However, it is clear that the treatment of morbid obesity needs to be recognized as a fundamental aspect in tackling the obesity epidemic. A strategy to develop bariatric care in Ireland seems warranted, given the previously established efficacy and cost-effectiveness of bariatric surgery. This effective intervention increases life-expectancy and increases the odds of diabetes remission, leading to a reduction in direct healthcare expenditure [9]. The challenge will be to implement a strategy that can show a return on investment within 3 years, but which will have an acceptable budget impact in the first year [14]. This may be achieved by focusing on those patients who would benefit most from surgery while simultaneously having the highest direct healthcare cost, such as those with established complications of diabetes (criteria two) who are using expensive drugs to treat their diabetes. Our findings demonstrate that by increasing the rates of surgery in Ireland in line with other European countries, such as France (57/100,000 people), the intervention will be more accessible, at least, to this population subgroup [16].

One strength of this study is the large national population-based sample. The objective measurement of BMI reduces the potential for misclassification bias. The data are weighted to adjust for differential nonresponse, minimizing the potential for selection bias and improving the representativeness of the findings. A number of limitations should be noted, however. Firstly, the reliance on self-reported doctor diagnoses may introduce misclassification bias and result in inaccurate estimates. However, a number of studies have demonstrated that self-report is a suitable method to determine the prevalence of T2D, hypertension, and previous MI compared with accessing medical records [24,25]. The self-reported doctor diagnosis of diabetes may underestimate the true prevalence of T2D as it does not measure undiagnosed diabetes. However, the prevalence of undiagnosed diabetes is low in this cohort [26]. Moreover, such an underestimation in the prevalence of diabetes would likely lead to an underestimation of the true prevalence of eligibility for bariatric surgery also. As there was no validated measure for sleep apnea in TILDA, our assessment of its prevalence is relatively crude and may have lacked adequate specificity. However, sleep apnea prevalence, using this measure, was similar to prevalence estimates in other cohorts of older adults [27,28]. Moreover, a sensitivity analysis, whereby sleep apnea was omitted from the eligibility criteria, showed no significant difference in the prevalence of eligibility for surgery. Thus, our estimates of the prevalence of bariatric surgical eligibility are likely to be conservative and clearly limited to those aged 50 years and older. The true numbers eligible for bariatric surgery in Ireland are likely to be higher.

Conclusions

Of older Irish adults, 7.97% are eligible for bariatric surgery according to recent guidelines. However, current service provision meets less than 0.1% of this need. These figures highlight the urgent need for the provision of clinical and cost-effective interventions to treat people with severe obesity. Our findings ought to be considered by policy-makers and should be used to guide resource allocation. One strategy to limit the budget impact is to focus on the 0.97% of patients, eligible under criteria two, who would see very large and immediate impacts on their health and healthcare cost. The provision of bariatric surgery to those in greatest need has the potential to improve both patient outcomes and reduce direct healthcare expenditure quickly.

Authors' contributions

K. O'Neill contributed to the study design, conducted data analysis and prepared the manuscript. F. Finucane, C. le Roux, and A. Fitzgerald contributed to the study design and revised the manuscript. P. Kearney designed the study and revised the manuscript. All authors have given final approval of the version to be published and agree to be accountable for all aspects of the work.

Acknowledgments

K. O'Neill and P. Kearney are funded by the Health Research Board Research Leader Award (RL/2013/7). The authors would like to thank Trinity College Dublin for the use of the TILDA data set and all of the TILDA participants.

References

[1] NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in diabetes since 1980: A pooled analysis of 751 population-based studies with 4.4 million participants. Lancet 2016;387 (10027):1513–30.

[2] Basterra-gortari FJ, Beunza JJ, Bes-Rastrollo M, Teledo E, Garcia-Lopez M, Martınez-Gonzalez MA. Increasing trend in the prevalence of morbid obesity in Spain: From 1.8 to 6.1 per thousand in 14 years. Rev Esp Cardiol 2011;64(5):424–6.

[3] Sturm R, Hattori A. Morbid obesity rates continue to rise rapidly in the United States. Int J Obes (Lond) 2013;37(6):889–91.

[4] Finucane MM, Stevens GA, Cowan MJ, et al. National, regional, and global trends in body-mass index since 1980: Systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. Lancet. 2011; 377(9765):557–67.

[5] Papasavas P, El Chaar M, Kothari SN, American Society for Metabolic and Bariatric Surgery Clinical Issues Committee. American Society for Metabolic and Bariatric Surgery position statement on vagal blocking therapy for obesity. Surg Obes Relat Dis 2016;12 (3):460–1.

[6] Rubino F, Nathan DM, Eckel RH, et al. Metabolic surgery in the treatment algorithm for type 2 diabetes: A joint statement by international diabetes organizations. Diabetes Care 2016; 39(7):861–77.

[7] Colquitt JL, Pickett K, Loveman E, Frampton GK. Surgery for weight loss in adults. Cochrane Database Syst Rev 2014;8: CD003641.

[8] Schauer P, Bhatt D, Kirwan J, et al. Bariatric surgery versus intensive medical therapy for diabetes. N Engl J Med 2014;371(7):682.

[9] Welbourn R, le Roux CW, Owen-Smith A, Wordsworth S, Blazeby JM. Why the NHS should do more bariatric surgery; how much should we do? BMJ 2016;353:i1472.

[10] Sjöström L. Review of the key results from the Swedish Obese Subjects (SOS) trial - a prospective controlled intervention study of bariatric surgery. J Intern Med 2013;273(3):219–34.

[11] Adams TD, Gress RE, Smith SC, et al. Long-term mortality after gastric bypass surgery. N Engl J Med 2007;357(8):753–61.

[12] Welbourn R, Small P, Finlay I, Sareela A, Somers S, Mahawar K. The United Kingdom National Bariatric Surgery Registry Second Report [monograph on the Internet]. Oxfordshire: Dendrite Clinical Systems Ltd; 2014. Available from: http://nbsr.co.uk/wp-content/uploads/2014/11/Extract_from_the_NBSR_2014_Report.pdf.

[13] Picot J, Jones J, Colquitt JL, et al. The clinical effectiveness and cost-effectiveness of bariatric (weight loss) surgery for obesity: a systematic review and economic evaluation. Health Technol Assess 2009;13 (41):1–190, 215-357, iii-iv.

[14] Klein S, Ghosh A, Cremieux PY, Eapen S, McGavock TJ. Economic impact of the clinical benefits of bariatric surgery in diabetes patients with BMI $\geq$35 kg/m^2. Obesity 2011;19(3):581–7.

[15] Keating CL, Dixon JB, Moodie ML, et al. Cost-Effectiveness of Surgically Induced Weight Loss for the Management of Type 2 Diabetes: Modeled Lifetime Analysis. Diabetes Care 2009;32 (4):567–74.

[16] Angrisani L, Santonicola A, Iovino P, Formisano G, Buchwald H, Scopinaro N. Bariatric Surgery Worldwide 2013. Obes Surg 2015;25 (10):1822–32.

[17] Buchwald H, Oien DM. Metabolic/bariatric surgery worldwide 2011. Obes Surg. 2013;23(4):427–36.

[18] OECD. Health at a Glance: Europe 2014 [publication on the Internet]. OECD Publishing; 2014. Available from: http://dx.doi.org/10.1787/health_glance_eur-2014-en.

[19] Tracey ML, Gilmartin M, O'Neill K, et al. Epidemiology of diabetes and complications among adults in the Republic of Ireland 1998-2015: a systematic review and meta-analysis. BMC Public Health 2016;16:132.

[20] Tracey ML, McHugh SM, Buckley CM, Canavan RJ, Fitzgerald AP, Kearney PM. The prevalence of Type 2 diabetes and related complications in a nationally representative sample of adults aged 50 and over in the Republic of Ireland. Diabet Med 2016; 33(4):441–5.

[21] Kearney PM, Cronin H, O'Regan C, et al. Cohort Profile: The Irish Longitudinal Study on Ageing. Int J Epidemiol 2011; 40(August):877–84.

[22] Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 1991;14(6):540–5.

[23] Whelan BJ, Savva GM. Design and methodology of the Irish Longitudinal Study on Ageing. J Am Geriatr Soc 2013;61 (Suppl 2):265–8.

[24] Comino EJ, Tran DT, Haas M, et al. Validating self-report of diabetes use by participants in the 45 and up study: a record linkage study [monograph on the Internet]. BMC Health Serv Res 2013;13(1):481.

[25] Okura Y, Urban LH, Mahoney DW, Jacobsen SJ, Rodeheffer RJ. Agreement between self-report questionnaires and medical record data was substantial for diabetes, hypertension, myocardial infarction and stroke but not for heart failure. J Clin Epidemiol 2004;57 (10):1096–103.

[26] Leahy S, O' Halloran AM, O' Leary N, et al. Prevalence and correlates of diagnosed and undiagnosed type 2 diabetes mellitus and pre-diabetes in older adults: Findings from the Irish Longitudinal Study on Ageing (TILDA). Diabetes Res Clin Pract 2015; 110(3):241–9.

[27] Punjabi NM. The epidemiology of adult obstructive sleep apnea. Proc Am Thorac Soc 2008;5(2):136–43.

[28] Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: A population health perspective. Am J Respir Crit Care Med 2002;165(9):1217–39.

BMC Public Health

RESEARCH ARTICLE Open Access

Epidemiology of diabetes and complications among adults in the Republic of Ireland 1998-2015: a systematic review and meta-analysis

Marsha L. Tracey[1*], Michael Gilmartin[2], Kate O'Neill[1], Anthony P. Fitzgerald[1], Sheena M. McHugh[1], Claire M. Buckley[1,3], Ronan J. Canavan[4] and Patricia M. Kearney[1]

Abstract

Background: Accurate estimates of the burden of diabetes are essential for future planning and evaluation of services. In Ireland, there is no diabetes register and prevalence estimates vary. The aim of this review was to systematically identify and review studies reporting the prevalence of diabetes and complications among adults in Ireland between 1998 and 2015 and to examine trends in prevalence over time.

Methods: A systematic literature search was carried out using PubMed and Embase. Diabetes prevalence estimates were pooled by random-effects meta-analysis. Poisson regression was carried out using data from four nationally representative studies to calculate prevalence rates of doctor diagnosed diabetes between 1998 and 2015 and was also used to assess whether the rate of doctor diagnosed diabetes changed over time.

Results: Fifteen studies (eight diabetes prevalence and seven complication prevalence) were eligible for inclusion. In adults aged 18 years and over, the national prevalence of doctor diagnosed diabetes significantly increased from 2.2 % in 1998 to 5.2 % in 2015 ($p_{\text{trend}} \leq 0.001$). The prevalence of diabetes complications ranged widely depending on study population and methodology used (6.5–25.2 % retinopathy; 3.2–32.0 % neuropathy; 2.5-5.2 % nephropathy).

Conclusions: Between 1998 and 2015, there was a significant increase in the prevalence of doctor diagnosed diabetes among adults in Ireland. Trends in microvascular and macrovascular complications prevalence could not be examined due to heterogeneity between studies and the limited availability of data. Reliable baseline data are needed to monitor improvements in care over time at a national level. A comprehensive national diabetes register is urgently needed in Ireland.

Keywords: Ireland, Prevalence, Trends, Diabetes, Microvascular, Macrovascular, Adults, Epidemiology

Background

Diabetes is a serious global public health issue which has been described as the most challenging health problem in the 21st century [1, 2]. Cases of diabetes have progressively increased worldwide; between 1980 and 2008 there was a two-fold increase in the number of adults with diabetes [3]. Type 2 diabetes is the main driver of the epidemic, accounting for approximately 90 % of all cases [2]. The increasing burden of diabetes is driven primarily by rising levels of obesity and an ageing population [2, 4]. To date there is no national surveillance programme, or national population-based survey of diabetes in Ireland. Therefore it is difficult to quantify or monitor the impact of diabetes at a national level. Estimates from the International Diabetes Federation (2013) suggest that the prevalence of diabetes is in line with global trends. In 2000, the IDF estimated that the prevalence of diabetes was 3.2 % [5], this had increased to 6.5 % in 2013 [2].

* Correspondence: m.treacy@ucc.ie
[1]Department of Epidemiology and Public Health, University College Cork, Western Gateway Building, Cork, Republic of Ireland
Full list of author information is available at the end of the article

Diabetes places a significant burden of care on the individual, health care professionals and the wider health system [1, 6]. Individuals with diabetes are two to four times more likely to develop cardiovascular disease relative to the general population and have a two to five-fold greater risk of dying from these conditions [7, 8]. Diabetes is a significant cause of blindness in adults, non-traumatic lower limb amputations and end-stage renal disease resulting in transplantation and dialysis [2].

Understanding the epidemiology of diabetes is essential to identify public health priorities. Accurate estimates of the burden of diabetes are essential for future planning and evaluation of services. While the IDF provides prevalence estimates for countries and regions, there are substantial variations in time trends as estimates are based on imputations [9, 10]. To date, estimates of diabetes prevalence in Ireland have been largely based on data from the 2007 National Survey of Health and Lifestyles in Ireland (SLÁN) [11]. Country specific prevalence rates have also been reported in the grey literature [2]; however these estimates have been extrapolated using data from the UK. The Euro Diabetes Index (2014) stated that there was a lack of reliable data to monitor diabetes related complications in Ireland [12]. To date, a comprehensive overview of the diabetes situation in Ireland has not been carried out. Therefore the rationale for carrying out this systematic review is to provide a comprehensive understanding of the diabetes situation in Ireland and to highlight current gaps in existing knowledge to inform future research. The aims of this review are (1) to systematically identify and summarise studies describing the prevalence of diabetes and the most common microvascular (retinopathy, neuropathy and nephropathy) and macrovascular complications among adults in Ireland between 1998 and 2014; and (2) to explore trends in diagnosed diabetes prevalence between 1998 and 2015.

Methods

This review was produced according to Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines for systematic reviews and meta-analyses [13]. Key words and study eligibility criteria were determined a priori.

Search strategy

Both peer-reviewed journal articles and reports were considered for this review. A systematic literature search was carried out in PubMed and Embase databases to identify relevant studies reporting the prevalence of diabetes, microvascular or macrovascular complications among adults within the Republic of Ireland. Keywords and Medical Subject Headings (MeSH) terms included Ireland, prevalence, diabetes, microvascular, retinopathy, neuropathy, nephropathy, macrovascular and cardiovascular disease. Keywords were combined using the AND or OR operators (Additional file 1). Titles and abstracts of the resulting literature were screened for further consideration. Reference lists of articles were also examined to identify potentially relevant studies. In addition, a Google search was conducted using the keywords prevalence, diabetes, retinopathy, neuropathy, nephropathy and Ireland to identify relevant grey literature. Searches were carried out between January 2014 and March 2014. A second search was carried out in December 2015 to ensure the review included all up to date relevant information.

Inclusion criteria

Studies were eligible for inclusion if they met the following criteria: (1) conducted in the Republic of Ireland between 1998 and 2014; (2) cross-sectional study design or baseline data from longitudinal studies; (3) prevalence estimates reported for adults aged ≥ 18 years, including men and women; (4) data provided on diabetes prevalence (including a self-report of a previous doctor diagnosis and undiagnosed diabetes) and/or the prevalence of microvascular complications (retinopathy, neuropathy, nephropathy) or macrovascular complications (myocardial infarction, congestive heart failure, stroke or TIA) in persons with diabetes; (5) if prevalence data were not reported, sufficient detail to calculate the numerator and denominator was provided; (6) the total sample size was ≥ 200; (7) adequate information was reported on the methods used.

Exclusion criteria

Studies containing participants from Northern Ireland, restricted to a specific sub-population (including hospital-based studies), solely focused on type 1 diabetes, pre-diabetes or gestational diabetes were excluded from this review. Model estimates of prevalence were also excluded. If multiple articles provided information on a single study, the article detailing the most comprehensive data was selected. Full text articles were retrieved for all potentially eligible studies and were independently reviewed by three authors (MT, MG, and KON).

Data abstraction and quality assessment

For each eligible study, three reviewers (MT, MG, and KON) individually collected relevant information using a structured data extraction form. The methodological quality of each included study was assessed using a critical appraisal checklist for studies used in systematic reviews addressing questions of prevalence [14]. This appraisal tool was developed to specifically examine the internal and external validity of prevalence data included in systematic reviews. Methodological quality was considered 'low' if three or less criteria were met, 'moderate' if four to six criteria were met and 'high' if seven to nine criteria were met. Articles were not excluded on the basis of quality. Any inconsistencies in data abstraction and quality assessment between reviewers were resolved through consensus.

Statistical analysis

A meta-analysis was carried out using STATA version 13.1 (StataCorp, College Station, TX, USA). Studies were grouped into four categories: diagnosed diabetes among adults aged 18+ years; diagnosed and undiagnosed diabetes among adults aged 45+ years; diagnosed diabetes among adults aged 45+ years; undiagnosed diabetes among adults aged 45+ years. Pooled estimates of diabetes prevalence and 95 % confidence intervals (95 % CI) were calculated. Trends in pooled prevalence could not be explored as there was a lack of available data from different time points; therefore an overall estimate was provided for each group. Heterogeneity between studies was assessed by the Chi-square based Q test and I^2 statistic. Potential publication bias was evaluated by the Begg's test. A two-tailed p <0.05 was regarded to be statistically significant. High heterogeneity was found among studies reporting diabetes prevalence ($I^2 \geq 75$ %, p-value < 0.01) hence, pooled estimates were calculated using random-effects model using the method of DerSimonian and Laird [15]. The results from the meta-analysis were presented in a forest plot. To determine the robustness of the results, a sensitivity analysis, based on high quality studies, was carried out. A meta-analysis of the prevalence of diabetes complications was inappropriate; factors which influence prevalence estimates (e.g. time since diabetes diagnosis, type of diabetes, method of diagnosis) either varied between studies or were not reported. Instead a narrative synthesis provides a summary of relevant data.

Trends in diagnosed diabetes

As trends in diabetes prevalence could not be calculated by meta-analysis, original datasets from four national population based studies [16–19], identified during the literature search were obtained and analysed. In each dataset, diabetes was defined by a self-report of a previous doctor diagnosis. A detailed description on study methodology can be found elsewhere [18, 20]. Using data from these national surveys, multivariate Poisson regression models were undertaken to impute annual gender and age-specific (18–39 years, 40–69 years, ≥70 years) rates of diagnosed diabetes and to assess trends over time. The dependent variable was the number of cases of diagnosed diabetes and the exposure variables were year of data collection and age group. An interaction term between calendar year and age group was considered to explore whether the rates of change over time differed across age groups; a non-significant interaction indicated a common linear trend in prevalence. The predict command was used post analysis to calculate the expected rates of diagnosed diabetes for each calendar year of the study. The gender and age-specific predicted rates were applied to 2004–2015 population data so the absolute number of diabetes cases could be obtained. Annual population estimates were obtained from the Central Statistics Office (CSO), Ireland [21]. A census took place in Ireland in 2002, 2006 and 2011; data for other study years were CSO inter-censal estimates [21]. Prevalence was calculated by dividing the number of expected cases of doctor diagnosis of diabetes by the total study population and was expressed as a percentage with 95 % CI. Prevalence estimates were presented graphically in Excel.

Results

Study selection

Results of the literature search and the selection process are summarised in Fig. 1. One report [22] provided two estimates for diabetes prevalence from two separate studies [16, 17]. In total, 15 studies were eligible for inclusion; eight reporting estimates on diabetes prevalence and seven reporting estimates on complication prevalence. Of the included studies, the methodological quality was considered moderate in nine studies and high in the remaining studies (Additional file 2).

Characteristics of selected studies

Characteristics of studies that reported the prevalence of diabetes or diabetes complications are presented in Tables 1 and 2. In all included studies, data collection were carried out between 1998 and 2011. Studies varied in terms of the study design, setting (national vs. regional), sampling approach and study quality. Of the 8 studies reporting on diabetes prevalence (Table 1), five articles had been published in peer-reviewed journals [11, 23–26], while three estimates were reported in two national reports [22, 27]. Of the 7 studies reporting diabetes complications (Table 2), six had been published in peer-reviewed journals [28–33], while one audit [34] provided data on the prevalence of diabetes related complications. Five studies utilised an objective data source to ascertain the prevalence of complications [28–30, 33, 34]. The diagnostic criteria for complications was unclear in three studies [31, 31, 34] whereas the remaining four used validated diagnostic criteria to identify cases [28–30, 33], however these criteria differed between studies reporting on the same complication.

Prevalence of diabetes in included studies

Table 3 reports the prevalence of diabetes by study. Individual and summary estimates, based on a random-effects meta-analysis are illustrated in Fig. 2. There was significant heterogeneity in all groups. Sensitivity analysis only

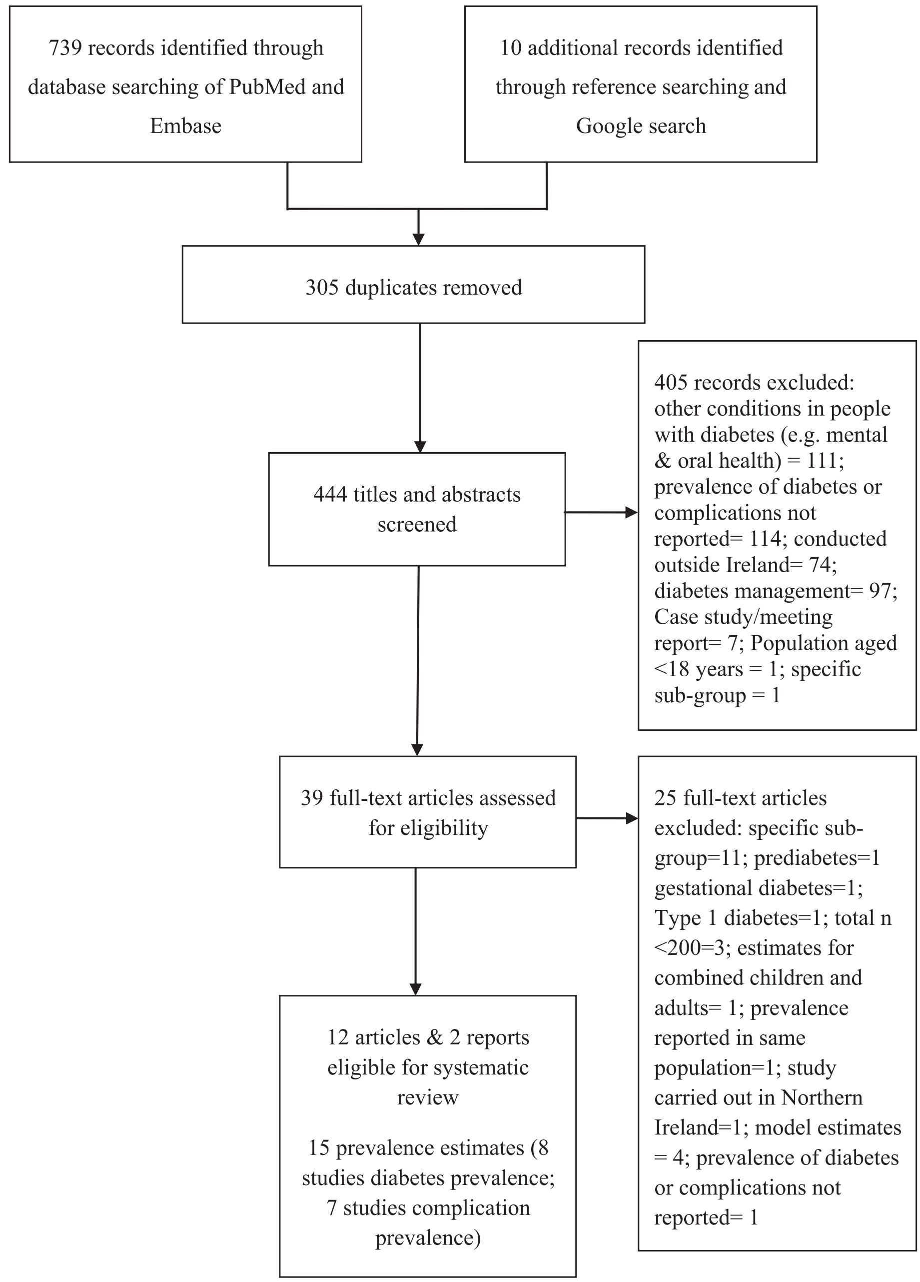


Fig. 1 PRISMA flow chart depicting the selection process of articles included in the systematic review

showed lower heterogeneity in combined prevalence rates for undiagnosed and diagnosed diabetes among adults aged over 45 years ($I^2 \geq 25$ %, $p = 0.36$); with a pooled prevalence of 9.2 % (95 % CI: 8.6–9.8) (Additional file 3). According to the Egger's test, there was no evidence of publication bias ($p = 0.27$).

Trends in the prevalence of diagnosed diabetes over time

In adults aged 18 years and over, the prevalence of diagnosed diabetes increased from 2.2 % (95 % CI: 1.7 %–2.7 %) in 1998 to 5.2 % (95 % CI: 5.1 %–5.3 %) in 2015 (p_{trend} = <0.001); representing an absolute mean increase of 0.17 % per year. In 2015, the incidence of diagnosed diabetes was 0.2/100 population.

Figure 3 illustrates the age-specific prevalence of self-reported diagnosed diabetes from 1998 to 2015. In adults aged between 18 and 39 years, the prevalence of self-reported doctor diagnosed diabetes remained stable between 1998 and 2015 in both men and women; p_{trend} >0.05. However, there was a significant increase in

Table 1 Characteristics of studies reporting the prevalence of diabetes or related complications among adults in the Republic of Ireland, 1998–2011

Author	Year of data collection	Study design	National or regional	Setting	Population	Sampling frame	Sampling method	Sample size	Males (%)	Age (years)	Study quality (out of 9)
Diabetes prevalence											
Sheily and Kelleher [22]	1998	Cross-sectional	National	Household	General population	Electoral register	Multistage sample	1632	47.7	55	7
Creagh et al. [23]	1998	Cross-sectional	Regional	17 GP practices	Primary Care Patients	Practice list	Stratified random	1018	48.2	50–69	6
Census Statistic Office (CSO) [27]	2001	Survey	National	Household	General population	Census	Total sample	3917203	-	18	5
Sheily and Kelleher [22]	2002	Cross-sectional	National	Household	General population	Electoral register	Multistage sample	1745	41.7	55	7
Balanda et al. [11]	2007	Cross-sectional	National	Household	General population	Geodirectory	Multistage probability	10,364	49.5	18	8
Gallagher et al. [24]	2009-2010	Cross-sectional	National	Database	Patients covered by GMS, LTI, DPS schemes	HSE-PCRS pharmacy claims data base	Total sample 2009 2010	3493974 3490877	-	16	6
Leahy et al. [25]	2009-2011	Cross-sectional analysis of longitudinal study	National	Household & designated health centre	General population	Geodirectory	Multi-stage probability	5377	46.5	50	8
OConnor et al. [26]	2010-2011	Cross-sectional	Regional	Primary care centre	Patients	Practice list	Random	2047	49.2	50–69	8

Table 2 Characteristics of studies reporting the prevalence of diabetes or complications among adults in the Republic of Ireland, 1998-2011

Author	Year of data collection	Study design	National or regional	Setting	Population	Sampling frame	Sampling method	Sample size	Males (%)	Age (years)	Study quality (out of 9)
Complication prevalence											
Kelliher et al. [28]	2003	Cross-sectional	National	National Council for Blind Ireland (NCBI)	All person registered blind	NCBI database	Total sample	6826	-	Adults	8
Buckley et al. [29]	2009	Cross-sectional	National	Population	People with diabetes	Hospital In-Patient Enquiry (HIPE) dataset	Total sample	723551	-	20 years	9
Marsden et al. [34]	2008-2009	Audit	Regional	20 general practices	Patients with T1 & T2 DM registered with diabetes structure care programme	Practice patient list	Every second person from list	1071	51.9	63 (sd 13)	5
Hurley et al. [30]	2008-2009	Cross-sectional analysis of longitudinal study	Regional	General practices with diabetes nurse	Patients with T1 & T2 DM	Practice diabetes register	Researchers selected eligible participants	563	60	64 (sd 13.4)	6
Farrell & Moran [31]	2010	Cross-sectional	Regional	30 general practices	T2 DM	Diabetes imitative database	Stratified sampling	309	-	-	5
Tracey et al. [32]	2009-2011	Cross-sectional analysis of longitudinal study	National	Household	General population	Geodirectory	Multi-stage probability	8175	53	50	8
McHugh et al. [33]	2011	Cross-sectional	Regional	30 general practices	Patients with T1 & T2 DM	Practice patient list	All persons with T1&T2DM invited	1542	57.3	65 (sd 13)	7

Table 3 Prevalence of diabetes among adults in included studies, 1998-2011

Study	Year of data collection	Response rate (%)	Sample size	Age	Diabetes type	Diagnostic criteria	Estimate	Prevalence % (95 % CI)		
								Males	Females	Total
Sheily and Kelleher [22]	1998	62	1632	55 years	All	SR[a]	Diagnosed	6.1	4.3	5.4
Creagh et al. [23]	1998	69.1	1018	50–69 years	2	FPG[b]	Diagnosed	-	-	2.8
							Undiagnosed	-	-	1.2
							Total	-	-	3.9 (2.9–5.4)
							Total 65 years	13	7	-
CSO [27]	July- Sept. 2001	-	3917203	18 years	All	SR	Diagnosed			
							18 years	-	-	1.5
							65 years	1.7	1.4	4.5
Sheily and Kelleher [22]	2002	53	1745	55 years	All	SR	Diagnosed	8.0	5.1	6.4
Balanda et al. [11]	2007	62	10,364	18 years	All	SR or medication use or HbA1c[c]	Diagnosed			
							18–44 years	-	-	0.7 (0.5–0.9)
							45+ years	6.8 (5.7–7.9)	5.4 (4.3–6.6)	6.1 (5.5–6.9)
							Total 18 years	-	-	3.5 (3.1–3.9)
							Undiagnosed (45 years)	4.0 (1.6–6.3)	1.7 (0.3–3.0)	2.8 (1.4–4.1)
							Total (diagnosed & undiagnosed 45 years)	10.8 (8.2–13.4)	7.1 (5.3–8.9)	8.9 (7.3–10.5)
Gallagher et al. [24]	2009 2010	-	3493974 3490877	18 years	2	At least 1 prescription of diabetes medication	Diagnosed			
							2009	-	-	2.8
							2010	-	-	3.1
Leahy et al. [25]	2009–2011	62	5377	50 years	2	SR or medication use or HbA1c[c]	Diagnosed	-	-	8.6 (7.6–9.5)
							Undiagnosed	-	-	0.9 (0.6–1.1)
							Total (diagnosed & undiagnosed)	11.8 (10.3–13.3)*	7.3 (6.0–8.5)*	9.5 (8.5–10.4)
							50–59 years	5.1 (4.0–7.0)	4.0	5.0 (4.0–6.0)
							60–69 years	6.0 (5.0–8.0)	14.0 (11.0–16.0)	-
							70–79 years	12.0 (8.0–14.0)	17.0 (14.0–21.0)	-
							80+ years	10.0 (5.0–15.0)	25.0 (15.0–36.0)	16.0 (10.7–21.4)
OConnor et al. [26]	2010-2011	67.9	2047	50–69 years	2	SR or medication use or HbA1c[c]	Diagnosed	6.8*	3.1*	5.0 (4.1–6.0)
							Undiagnosed	7.1*	2.7*	3.5 (2.8–4.4)
							Total	11.1*	6.0*	8.5 (7.4–8.8)

*p for difference < 0.05
[a]*SR* self-reported data; [b]Fasting plasma glucose (American Diabetes Association criteria (ADA, 1997); [c]HbA1c (ADA, 2010)

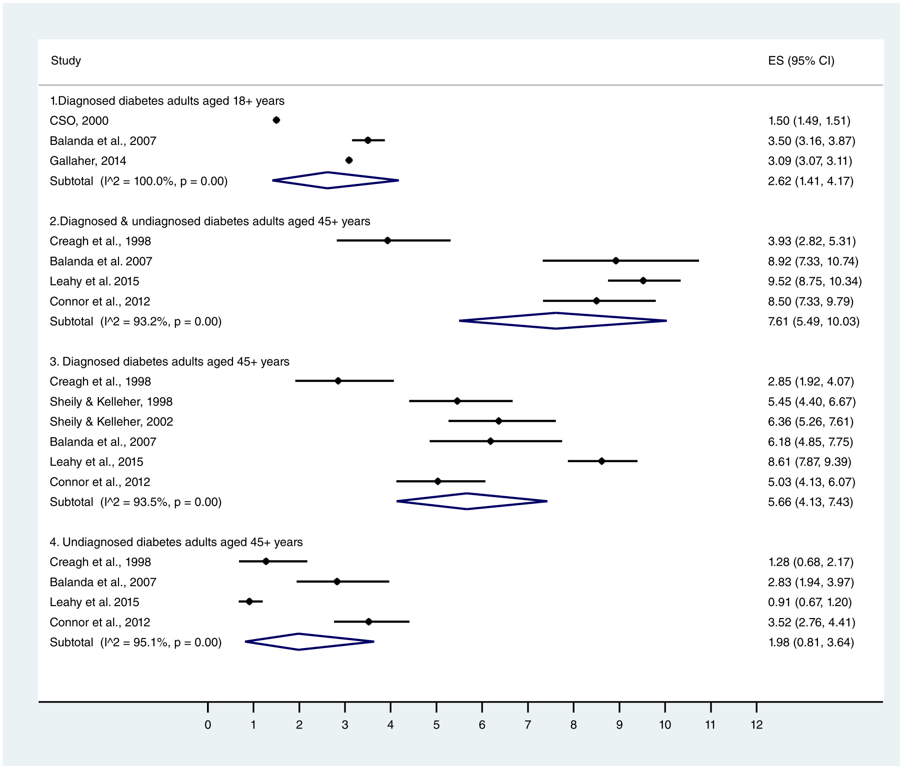


Fig. 2 Forest plot of individual and summary diabetes prevalence estimates of included studies

prevalence among men aged 40 to 69 years between 1998 (3.5 % [95 % CI: 3.4–3.6 %]) and 2015 (6.6 % [95 % CI: 6.5–6.7 %]; p_{trend} <0.001). The prevalence of diabetes also increased among women in the same age group over the same time period (1998–2.5 % [95 % CI: 2.4–2.5 %] to 2015- 4.2 % [95 % CI: 4.1–4.3 %]; p_{trend} <0.001). In those aged 70 years and over, an upward trend in prevalence among both men (1998–8.2 % [95 % CI: 8.0–8.3 %] to 2015- 15.1 % [95 % CI: 14.8–15.2 %]) and women (1998- 4.7 % [95 % CI: 4.5–4.8 %]

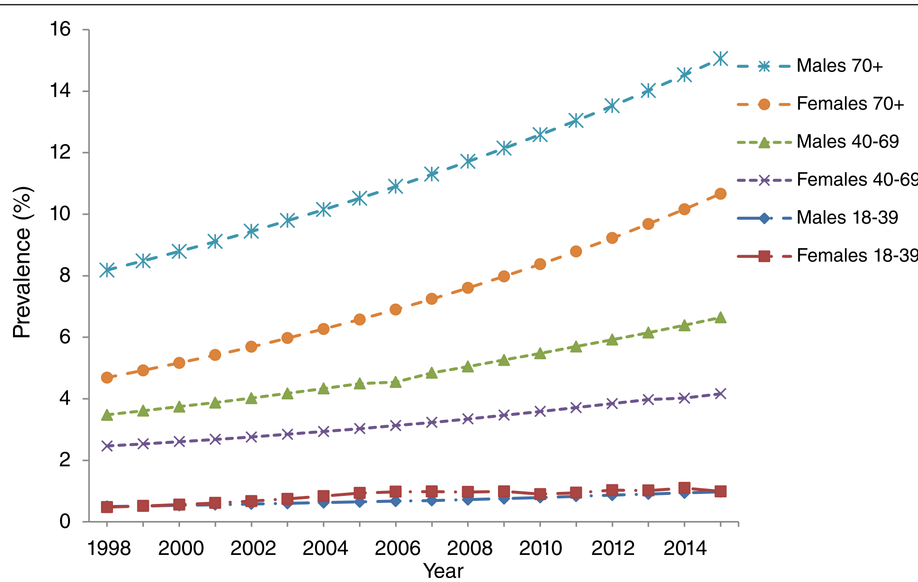


Fig. 3 Prevalence of self-reported doctor diagnosed diabetes among adults in RoI, 1998–2015

to 2015- 10.7 % [95 % CI: 10.5–10.8 %]) was also observed; p_{trend} <0.001.

Prevalence of microvascular and macrovascular complications

Table 4 describes the prevalence of microvascular and macrovascular complications in each included study. Five out of seven studies reported the prevalence of retinopathy [27, 29–31, 33]. Among people with type 2 diabetes, a population based study reported the prevalence of diabetic retinopathy to be 8.5 % in 2009–2011 [30]; a regional study, carried out among primary care patients, found a higher prevalence of 24.8 % [31]; however this estimate included patients with type 1 and 2 diabetes and was based on objective data. A similar estimate (25.6 %) was reported in a comparable cohort of primary care patients in a different region [33].

In terms of diabetes-related neuropathy, a divergence in the reported prevalence between studies was also observed. Data from 12 primary care centres in the West of Ireland indicated a prevalence of past documented neuropathy to be 3 % [30]. On the other hand, a population-based study reported a prevalence of 14.6 % [32]. These patients had similar average duration since diagnosis (7.8 years [30] vs. 5.0 years [32]); however, the latter estimate was based on self-reported data. Prevalence rates for leg amputations were 1.7 % among primary care patients with diabetes [30]. In contrast, the prevalence of non-traumatic lower leg amputation was lower (0.2 %) in a population-based study which utilised national hospital discharge data [29].

With reference to nephropathy, prevalence among those with type 2 diabetes was similar in two studies [31, 32]. In the three studies presenting data on macrovascular complications, a marked difference in prevalence was observed. A primary care audit reported a prevalence of 3.5 % in patients with type 1 and 2 diabetes [34]. In contrast, among those with type 2 diabetes, a population based study reported a higher prevalence of 15.1 % [32].

Discussion

This systematic review is the first study to compile all available evidence reporting the prevalence of diabetes (diagnosed and undiagnosed) and related complications (microvascular and macrovascular) among adults in Ireland between 1998 and 2015. Fifteen studies (eight describing diabetes prevalence and seven describing complication prevalence) were included.

Similar to other systematic reviews [35–37]; comparability between studies was limited due to differences in study population, sampling methods and diagnostic criteria. Additionally, substantial statistical heterogeneity was detected between studies reporting the prevalence of diabetes; therefore our pooled estimates have to be interpreted with caution. Sensitivity analysis, based on study quality, lowered the heterogeneity of combined prevalence rates for undiagnosed and diagnosed diabetes among adults aged over 45 years. However, this may reflect variability between prevalence estimates rather than study quality. Trends in diabetes prevalence could not be explored by meta-analysis, therefore, original data from four population-based national studies [16–19] were obtained to explore time trends in doctor diagnosed diabetes prevalence between 1998 and 2015. Over a seventeen year period, we observed an important increase in the national prevalence of self-reported diagnosed diabetes in Ireland.

Consistent with previous research [38–40] trends in the prevalence of self-reported diagnosed diabetes remained constant in adults aged 18 to 39 years, while an increasing prevalence was observed in the older age groups. We were unable to distinguish between the various types of diabetes in this review; however it can be assumed that type 2 diabetes is driving the increase in prevalence as it accounts for 90 % of all diabetes cases [1, 2]. The prevalence of diabetes was consistently higher in males compared to females. Evidence suggests that men are at a higher risk of developing type 2 diabetes as they develop diabetes at a lower BMI, are more predisposed to central fat deposition and are more prone to insulin resistance [41]. Therefore, men are more likely to develop type 2 diabetes in response to increasing levels of obesity [42]. On the other hand, the higher prevalence in the male population may reflect preferences in diagnostic methods. Evidence has highlighted that the prevalence of FPG diagnosed diabetes is higher among men, whereas women are more commonly diagnosed by a 2-h plasma glucose test [43]. While it is not possible to determine the method of diabetes diagnosis in this review; it is important to consider how these gender differences may influence diagnosed diabetes prevalence estimates over time.

Similar to diagnosed diabetes, trends in the prevalence of undiagnosed diabetes could not be explored by meta-analysis as only two nationally representative studies had relevant data [11, 25]. The prevalence of undiagnosed diabetes, based on HbA1c, decreased from 2.8 % in 2007 to 0.9 % in 2009–2011 among adults aged ≥45 years and ≥50 years, respectively. While the prevalence of diagnosed diabetes increased from 6.1 % in 2007 [11] to 8.6 % in 2009–2011 [25]. This shift from undiagnosed to diagnosed diabetes prevalence has also been observed in a study carried out in Germany [10]. This decrease in undiagnosed diabetes prevalence may be attributable to earlier detection of diabetes [10]. In Ireland, screening high risk patients for type 2 diabetes has been encouraged since the introduction of national guidelines for diabetes-care in 2002 [44]. Another study based on 29144 adults aged 45–75 years with private health insurance, reported the prevalence of undiagnosed diabetes to be 1.8 % in

Table 4 Prevalence of microvascular and macrovascular complications in included studies, 2003–2011

Author	Year of study	Response rate (%)	Sample size	Age	Diabetes type	Time since diabetes diagnosis	Data source	Diagnostic method	Type of complication	Prevalence (%) Total
Kelliher et al. [28]	2003	-	6826	Adults	All	-	National blind registry	Visual acuity of <6/60 in better eye/visual field subtending angle of 20°/< less	Blindness due to diabetic retinopathy	4.7
Buckley et al. [29]	2009	-	723,551	20 years	All	-	Hospital discharge data	ICD-10 codes	Non-traumatic lower leg amputation	0.2
Marsden et al. [34]	Nov 2008-March 2009	72	1071	63 years (sd 13)	T1: 7.5 % T2: 92.3 %	15 years	Electronic & paper clinical notes & referral letters	- Risk classification score ACR 2.5–25 ACR >25 - - - -	Diabetic retinopathy Foot ulcer Microalbuminuria Proteinuria Myocardial Infarction Heart Failure Transient Ischemic Attack Stroke Total macrovascular	24.8 2.5 32.1 6.0 0.4 0.3 1.5 0.5 3.5
Hurley et al. [30]	Feb 2008-Sept 2009	68	563	64 years (sd 13.4)	T1: 10 % T2: 90 %	7.7 (8.2) years	Clinical foot examination & practice medical records	Scottish Intercollegiate Guidelines Network risk stratificationsystem & previous doctor diagnosis	Documented diabetic neuropathy Foot ulceration Past amputation Neuropathy symptoms at examination	3.0 3.7 1.7 32
Farrell & Moran [31]	2010	-	309	-	T2	-	Chart review	-	Diabetic retinopathy Neuropathy Peripheral vascular disease Chronic kidney disease Cerebrovascular disease	6.5 12.3 12.9 5.5 5.2
Tracey et al. [32]	2009–2011	62	655	50 years	T2	5 (IQR 3–10) years	SR previous doctor diagnosis	-	Diabetic retinopathy Neuropathy Leg ulcer Nephropathy Proteinuria Total macrovascular	8.2 (6.2–10.9) 14.6 (11.4–18.2) 4.2 (2.8–6.4) 5.1 (3.4–7.6) 6.1 (4.3–8.6) 15.1 (12.2–18.4)
McHugh et al. [33]	2011	GP = 94 %; Screening uptake = 43 %	1542	65 years (sd 13)	T1: 4.9 % T2: 85.6 %	-	Eye examination & clinical records	Fundus 45° digital PASA-approved camera	Background (R1) Pre proliferative (R2) Proliferative (R3) Any diabetic retinopathy	21.5 (19.5–23.6) 3.4 (2.6–4.5) 0.7 (0.4–1.3) 25.6 (23.5–27.9)

2009–2012 [45]. However this estimate was derived from FPG; evidence suggests that the use of HbA1c may underestimate diabetes prevalence compared with estimates using FPG [38, 43, 46].

The prevalence of diabetes complications varied substantially between studies therefore comparisons between studies have to be interpreted with caution. These variations may be attributable to differences in disease duration or study population (type 1 and type 2 diabetes vs. type 2 diabetes), study setting (primary care vs. population-based) or heterogeneity in the criteria used to diagnose macrovascular and microvascular complications. Objective data describing the national prevalence of diabetic retinopathy was not available however, regional data on diabetic retinopathy showed that approximately 25 % of primary care patients with type 1 and type 2 diabetes had been diagnosed with this condition [33, 34]. This estimate is higher than a previous hospital-based study based on patients with type 2 diabetes (14.8 %) [47] and primary care data from the UK (19.6 %) [48] but lower than global prevalence estimates (34.6 %) [49]. Though, caution has to be applied when interpreting the results as both regional studies included in this review reported a low uptake rate of retinopathy screening at approximately 50 % [33, 34]. Additionally, characteristics between attenders and non-attenders were not compared in either study; hence it is possible that there were systematic differences between the two groups. Healthier people are more likely to participate in research; therefore the prevalence of diabetic retinopathy may have been underestimated. As a national screening programme for diabetic retinopathy was introduced in 2013 [50], future estimates based on this national programme may be more reliable.

Limitations

The strengths and limitations of this systematic review should be noted. Both peer-reviewed articles and estimates detailed in the grey literature were included to limit the impact of publication bias. Original data from four national studies were obtained so trends in diagnosed diabetes prevalence could be examined over a 17 year period. Although response rates were below the optimal rate of 70 %, the representativeness of each study has been demonstrated previously [18, 51], so it can be assumed that the results presented can be generalised to the Irish population.

However, several limitations need to be acknowledged. Firstly, studies included in this review were of moderate to high quality; however, six of the included studies relied on self-reporting to determine the prevalence of diagnosed diabetes and one study relied on self-reporting to determine the prevalence of diabetes related complications. This approach is prone to misclassification bias which can result in an inaccurate estimation of prevalence [52]. When compared to medical records, data from self-report have been shown to underestimate the prevalence of diabetic retinopathy [53]. However, moderate to high levels of agreement between diabetes prevalence and self-report have been shown in several studies [54–56]. Although only data on self-reported diabetes were available, results from trend analysis are in line with other developed countries. Secondly, without the inclusion of undiagnosed diabetes in our trend analysis, we acknowledge that diabetes prevalence is underestimated. Finally, significant increases in diagnosed diabetes prevalence were observed over time but these increases may be attributed to heightened awareness among patients, changes in clinical practices, including increased screening for type 2 diabetes, and better survival rates for patients with diabetes [57]. However, there is a lack of data on mortality rates among people with diabetes in Ireland; therefore it is not possible to determine whether our increasing trends in prevalence are due to improved health outcomes in those with diabetes.

Conclusion

This review provides the first comprehensive overview of the burden of diabetes in Ireland. In the absence of a national diabetes register, the findings in this review provide a robust estimate of the trends in prevalence of doctor diagnosed diabetes among the adult population in Ireland. Findings from this review are in accordance with the Euro Diabetes Index (2014) [12]; there is a lack of information relating to the prevalence of undiagnosed diabetes, macrovascular and microvascular complications. Interpretation of available data was limited due to inconsistencies in reporting, limited availability of objective data and standardisation in diagnostic criteria. We suggest that the true burden of diabetes in Ireland is underestimated [58]. In 2010, the National Clinical Programme in Diabetes was established to improve and standardise patient care in Ireland [59]. Reliable baseline data are needed to monitor improvements in care over time at a national level. Therefore, we suggest that a comprehensive national diabetes register is urgently needed in Ireland.

Additional files

Additional file 1: Electronic search strategies for articles. (DOCX 11 kb)

Additional file 2: Critical appraisal checklist for studies reporting prevalence data. (DOCX 25 kb)

Additional file 3: Sensitivity analysis based on high quality studies. (DOCX 16 kb)

Competing interest

The authors declare that they have no competing interests.

Authors' contributions

MLT, MG, PMK, APF conceived and designed the study. MLT, MG, KON researched data. MLT analysed the data. MLT wrote the manuscript. PMK, SMMc, CMB, APF, RJC, KON, APF reviewed the manuscript. MLT edited the manuscript. MLT, MG, KON, PMK, SMMc, CMB, APF, RJC approved final manuscript.

Acknowledgements
Marsha Tracey and Professor Patricia Kearney are funded by the Health Research Board Leadership Award in Diabetes (RL/2013/7). Dr. Sheena Mc Hugh is funded by the Centre for Ageing and Development Research in Ireland (CARDI) Leadership Fellowship. MLT would like to thank Professor John Browne, University College Cork for advice on methodology.

Author details
[1]Department of Epidemiology and Public Health, University College Cork, Western Gateway Building, Cork, Republic of Ireland. [2]Department of Medicine, Royal College of Surgeons, Dublin, Republic of Ireland. [3]Department of Public Health, Heath Service Executive (HSE) South, Cork, Republic of Ireland. [4]Department of Endocrinology, St. Vincent's University Hospital, Dublin, Republic of Ireland.

Received: 6 July 2015 Accepted: 3 February 2016
Published online: 09 February 2016

References

1. Zimmet P, Alberti KG, Shaw J. Global and societal implications of the diabetes epidemic. Nature. 2001;414:782–7.
2. International Diabetes Federation. IDF Diabetes Atlas, 6th edn. International Diabetes Federation. Brussels, Belgium: 2013.
3. Danaei G, Finucane MM, Lu Y, Singh GM, Cowan MJ, Paciorek CJ, et al. National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2·7 million participants. Lancet. 2011;378:31–40.
4. Kearns K, Dee A, Fitzgerald A, Doherty E, Perry IJ. Chronic disease burden associated with overweight and obesity in Ireland: the effects of a small BMI reduction at population level. BMC Public Health. 2014;14:143.
5. International Diabetes Federation. Diabetes Atlas, 2000, 1st edn. International Diabetes Federation. Brussels, Belgium: 2000.
6. Venkat Narayan KM, Greg EW, Fagot-Campagna A, Engelgau MM, Vinicor F. Diabetes- a common, growing, serious, costly and potentially preventable public health problem. Diabetes Res Clin Pract. 2000;50:S77-S84.
7. Garcia MJ, McNamara PM, Gordon T, Kannell WB. Morbidity and mortality in diabetics in the framingham population: Sixteen year follow-up study. Diabetes. 1974;23:105–11.
8. Roper NA, Bilous RW, Kelly WF, Unwin NC, Connolly VM. Cause-specific mortality in a population with diabetes: South Tees Diabetes Mortality Study. Diabetes Care. 2002;25:43–8.
9. Tamayo T, Rosenbauer J, Wild SH, Spijkerman AM, Baan C, Forouhi NG, et al. Diabetes in Europe: an update. Diabetes Res Clin Pract. 2014;103:206–17.
10. Heidemann C, Du Y, Paprott R, Haftenberger M, Rathmann W, Scheidt-Nave C. Temporal changes in the prevalence of diagnosed diabetes, undiagnosed diabetes and prediabetes: findings from the German health interview and examination surveys in 1997–1999 and 2008–2011. Diabetic Med. 2015. doi:10.1111/dme.13008.
11. Balanda KP, Buckley CM, Barron SJ, Fahy LE, Madden JM, Harrington JM, et al. Prevalence of diabetes in the Republic of Ireland: Results from the National Health Survey (SLAN) 2007. PLoS One. 2013;8:e78406.
12. Garrofé B, Björnberg A, Yung Phang A. Euro diabetes index 2014. http://www.healthpowerhouse.com/files/EDI-2014/EDI-2014-report.pdf. Accessed 21 Oct 2014.
13. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med. 2009;151:264–9.
14. Munn Z, Moola S, Riitano D, Lisy K. The development of a critical appraisal tool for use in systematic reviews addressing questions of prevalence. Int J Health Policy Manag. 2014;3:123–8.
15. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986;7:177–88.
16. Department of Health and Children. Survey on Lifestyle and Attitude to Nutrition (SLÁN). Galway: NUIG, Centre for Health Promotion Studies; 1998.
17. Department of Health and Children. Survey on Lifestyle and Attitude to Nutrition (SLÁN). Galway: NUIG, Centre for Health promotion Studies; 2002.
18. Morgan K, McGee H, Watson D, Perry IJ, Barry M, Shelley E, et al. SLAN 2007: survey of lifestyle, attitudes & nutrition in Ireland: main report. Dublin: Department of Health and Children. http://epubs.rcsi.ie/cgi/viewcontent.cgi?article=1002&context=psycholrep. Accessed 10 January 2015.
19. Kearney PM, Cronin H, O'Regan C, Kamiya Y, Savva GM, Whelan B, et al. Cohort profile: The Irish longitudinal study on ageing. Int J Epidemiol. 2011;40:877–84.
20. Kenny R, Whelan B, Cronin H, Kamiya Y, Kearney P, O'Regan C, et al. The design of the Irish longitudinal study on ageing. Dublin: Trinity College Dublin; 2010.
21. Census of Population Interactive Tables, 2014. http://www.cso.ie/px/pxeirestat/Database/eirestat/Annual%20Population%20Estimates/Annual%20Population%20Estimates_statbank.asp?SP=Annual%20Population%20Estimates&Planguage=0. Accessed 2 March 2015.
22. Shiely F, Kelleher C. Older people in Ireland: A profile of health status, lifestyle and socio-economic factors from SLÁN: National Council on Ageing and Older People Dublin; 2004.
23. Creagh D, Neilson S, Collins A, Colwell N, Hinchion R, Drew C, et al. Established cardiovascular disease and CVD risk factors in a primary care population of middle-aged Irish men and women. Ir Med J. 2002;95:298–301.
24. Gallagher N, Bennett K, Smith SM, O'Reilly D. Impact of two different health systems on the burden of type 2 diabetes. J Health Serv Res Policy. 2014;19:69–76.
25. Leahy S, O'Halloran A, O'Leary N, Healy M, McCormack M, Kenny R, et al. Prevalence and correlates of diagnosed and undiagnosed type 2 diabetes mellitus and pre-diabetes in older adults: Findings from the Irish Longitudinal Study on Ageing (TILDA). Diabetes Res Clin Prac. 2015;110(3):241–9.
26. OConnor JM, Millar SR, Buckley CM, Kearney PM, Perry IJ. The prevalence and determinants of undiagnosed and diagnosed type 2 diabetes in middle-aged irish adults. PLoS One. 2013;8(11):e80504.
27. Central Statistics Office. Quarterly National Household Survey, 2001. Module on Health, Quarter 3. 2001. http://www.cso.ie/en/media/csoie/releases publications/documents/labourmarket/2001/qnhs_healthqtr32001.pdf. Accessed 14 March 2014.
28. Kelliher C, Kenny D, O'Brien C. Trends in blind registration in the adult population of the Republic of Ireland 1996-2003. Br J Ophthalmol. 2006;90:367–71.
29. Buckley CM, O'Farrell A, Canavan RJ, Lynch AD, De La Harpe DV, Bradley CP, et al. Trends in the incidence of lower extremity amputations in people with and without diabetes over a five-year period in the Republic of Ireland. PLoS One. 2012;7:e41492.
30. Hurley L, Kelly L, Garrow AP, Glynn LG, McIntosh C, Alvarez-Iglesias A, et al. A prospective study of risk factors for foot ulceration: The West of Ireland Diabetes Foot Study. QJM. 2013;106:1103–10.
31. Farrell C, Moran J. Comparison of comorbidities in patients with pre-diabetes to those with diabetes mellitus type 2. Ir Med J. 2014;107:72–4.
32. Tracey ML, McHugh SM, Buckley CM, Canavan RJ, Fitzgerald AP, Kearney PM. The prevalence of Type 2 diabetes and related complications in a nationally representative sample of adults aged 50 and over in the Republic of Ireland. Diabet Med. 2015. doi:10.1111/dme.12845.
33. McHugh SM, Buckley CM, Murphy K, Doherty S, O'Keeffe G, Alade J, et al. Quality-assured screening for diabetic retinopathy delivered in primary care in Ireland: an observational study. Br J Gen Pract. 2013;63:e134–40.
34. Marsden P, Brennan C, McHugh SM, Harkins V. Audit Report of the HSE Midland Diabetes StructuredCare Programme. Department of Public Health. Health Service Executive Dublin Mid-Leinster. 2010.
35. Pereira M, Carreira H, Lunet N, Azevedo A. Trends in prevalence of diabetes mellitus and mean fasting glucose in Portugal (1987-2009): a systematic review. Public Health. 2014;128:214–21.
36. Bos M, Agyemang C. Prevalence and complications of diabetes mellitus in Northern Africa, a systematic review. BMC Public Health. 2013;13:387.
37. Hall V, Thomsen RW, Henriksen O, Lohse N. Diabetes in Sub Saharan Africa 1999-2011: epidemiology and public health implications. A systematic review. BMC Public Health. 2011;11:564.
38. Hamer M, Kengne AP, Batty GD, Cooke D, Stamatakis E. Temporal trends in diabetes prevalence and key diabetes risk factors in Scotland, 2003-2008. Diabet Med. 2011;28:595–8.
39. Lipscombe LL, Hux JE. Trends in diabetes prevalence, incidence, and mortality in Ontario, Canada 1995-2005: a population-based study. Lancet. 2007;369:750–6.
40. Bonaldi C, Vernay M, Roudier C, Salanave B, Oleko A, Malon A, et al. A first national prevalence estimate of diagnosed and undiagnosed diabetes in

France in 18- to 74-year-old individuals: the French Nutrition and Health Survey 2006/2007. Diabet Med. 2011;28:583–9.
41. Sarwar N, Gao P, Seshasai SR, Gobin R, Kaptoge S, Di Angelantonio E, et al. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. Lancet. 2010;375:2215–22.
42. Sattar N. Gender aspects in type 2 diabetes mellitus and cardiometabolic risk. Best Pract Res Clin Endocrinol Metab. 2013;27:501–7.
43. Cowie CC, Rust KF, Byrd-Holt DD, Gregg EW, Ford ES, Geiss LS, et al. Prevalence of diabetes and high risk for diabetes using A1C criteria in the U.S. population in 1988-2006. Diabetes Care. 2010;33:562–8.
44. Clarke A. Diabetes care: Securing the future. Action plan for implementation of the St. Vincent declaration. Dublin: Diabetes Service Development Group; 2002.
45. Sinnott M, Kinsley BT, Jackson AD, Walsh C, O'Grady T, Nolan JJ, et al. Fasting plasma glucose as initial screening for diabetes and prediabetes in Irish adults: The Diabetes Mellitus and Vascular Health Initiative (DMVhi). PLoS One. 2015;10:e0122704.
46. Juarez DT, Demaris KM, Goo R, Mnatzaganian CL, Wong Smith H. Significance of HbA(1c) and its measurement in the diagnosis of diabetes mellitus: US experience. Diabetes Metab Syndr Obes. 2014;7:487-494.
47. Nolan JJ, O'Halloran D, McKenna TJ, Firth R, Redmond S. The cost of treating type 2 diabetes (CODEIRE). Ir Med J. 2006;99:307–10.
48. Ruta LM, Magliano DJ, Lemesurier R, Taylor HR, Zimmet PZ, Shaw JE. Prevalence of diabetic retinopathy in Type 2 diabetes in developing and developed countries. Diabet Med. 2013;30:387–98.
49. Yau JW, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, et al. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care. 2012;35:556–64.
50. Diabetic RetinaScreen. The National Diabetic Retinal Screen Programme. 2015. http://www.diabeticretinascreen.ie/. Accessed 12 Nov 2014.
51. Savva GM. In fifty plus in Ireland 2011: First results from the Irish longitudinal study on ageing. Dublin: Trinity College Dublin; 2011.
52. Critchfield T, Tucker J, Vuchinich R. Self-report methods. In: Lattal K, Perone M, editors. Handbook of research methods in human operant behavior. US: Springer; 1998. p. 435–70.
53. MacLennan PA, McGwin Jr G, Searcey K, Owsley C. Medical record validation of self-reported eye diseases and eye care utilization among older adults. Curr Eye Res. 2013;38:1–8.
54. Comino EJ, Tran DT, Haas M, Flack J, Jalaludin B, Jorm L, et al. Validating self-report of diabetes use by participants in the 45 and Up Study: a record linkage study. BMC Health Serv Res. 2013;13:481.
55. Okura Y, Urban LH, Mahoney DW, Jacobsen SJ, Rodeheffer RJ. Agreement between self-report questionnaires and medical record data was substantial for diabetes, hypertension, myocardial infarction and stroke but not for heart failure. J Clin Epidemiol. 2004;57:1096–103.
56. Galenkamp H, Huisman M, Braam AW, Schellevis FG, Deeg DJ. Disease prevalence based on older people's self-reports increased, but patient-general practitioner agreement remained stable, 1992-2009. J Clin Epidemiol. 2014;67:773–80.
57. Maruthur NM. The growing prevalence of type 2 diabetes: increased incidence or improved survival? Curr Diab Rep. 2013;13:786–94.
58. Kanavos P, van den Aardweg S, Schurer W. Diabetes expenditure, burden of disease and management in 5 EU countries. LSE Health and Social Care. 2012. http://www.lse.ac.uk/lsehealthandsocialcare/research/lsehealth/mtrg/lsediabetesreport26jan2012.pdf. Accessed 3 Nov 2014.
59. Health Service Executive. National Clinical Programme for Diabetes. 2010 http://www.hse.ie/eng/about/Who/clinical/natclinprog/diabetesprogramme/. Accessed 29 Aug 2014

McHugh et al. Implementation Science (2016) 11:107
DOI 10.1186/s13012-016-0464-9

Implementation Science

STUDY PROTOCOL

Open Access

Evaluating the implementation of a national clinical programme for diabetes to standardise and improve services: a realist evaluation protocol

S. McHugh[1*], M. L. Tracey[1], F. Riordan[1], K O'Neill[1], N. Mays[2] and P. M. Kearney[1]

Abstract

Background: Over the last three decades in response to the growing burden of diabetes, countries worldwide have developed national and regional multifaceted programmes to improve the monitoring and management of diabetes and to enhance the coordination of care within and across settings. In Ireland in 2010, against a backdrop of limited dedicated strategic planning and engrained variation in the type and level of diabetes care, a national programme was established to standardise and improve care for people with diabetes in Ireland, known as the National Diabetes Programme (NDP). The NDP comprises a range of organisational and service delivery changes to support evidence-based practices and policies. This realist evaluation protocol sets out the approach that will be used to identify and explain which aspects of the programme are working, for whom and in what circumstances to produce the outcomes intended.

Methods/design: This mixed method realist evaluation will develop theories about the relationship between the context, mechanisms and outcomes of the diabetes programme. In stage 1, to identify the official programme theories, documentary analysis and qualitative interviews were conducted with national stakeholders involved in the design, development and management of the programme. In stage 2, as part of a multiple case study design with one case per administrative region in the health system, qualitative interviews are being conducted with frontline staff and service users to explore their responses to, and reasoning about, the programme's resources (mechanisms). Finally, administrative data will be used to examine intermediate implementation outcomes such as service uptake, acceptability, and fidelity to models of care.

Discussion: This evaluation is using the principles of realist evaluation to examine the implementation of a national programme to standardise and improve services for people with diabetes in Ireland. The concurrence of implementation and evaluation has enabled us to produce formative feedback for the NDP while also supporting the refinement and revision of initial theories about how the programme is being implemented in the dynamic and unstable context of the Irish healthcare system.

Keywords: Realist evaluation, Protocol, Diabetes, Implementation

* Correspondence: s.mchugh@ucc.ie
[1]Department of Epidemiology & Public Health, Western Gateway Complex, University College Cork, Western Rd, Cork, Ireland
Full list of author information is available at the end of the article

Background

Diabetes is a major public health and health service challenge worldwide with global prevalence estimated to increase from 2.8 % in 2000 to 4.4 % in 2030, an increase from 171 million people to 366 million people in 30 years [1]. The most recent Global Burden of Disease study estimates that diabetes is the seventh leading cause of years lived with disability worldwide [2]. Diabetes is associated with reduced quality of life and life expectancy [3, 4]. There are also significant societal and health service costs associated with the condition; global health expenditure on diabetes was estimates to be at least US$376 billion in 2010, rising to US$490 billion by 2030 [5].

Optimal diabetes care

The need for organised coordinated implementation of strategies to improve diabetes care and reduce disease burden has long been recognised. In 1989, health departments from across Europe, including Ireland, signed the St. Vincent Declaration, a set of standards and goals to improve diabetes care [6]. The onus was placed on individual governments to implement strategies to meet the agreed targets. Over the next three decades, a number of countries developed national and regional multidimensional programmes to improve the monitoring and management of diabetes and to enhance the coordination of care within and across settings [7–10].

Consensus exists on what constitutes good quality diabetes care. Substantial evidence supports treatments to manage diabetes and slow the progression of complications [11–15]. National and international guidelines recommend the regular monitoring and management of blood glucose levels, blood pressure, kidney function, body mass index and smoking status, as well as routine foot surveillance, retinopathy screening and patient self-management education [16–18]. At a system level, the organisational features of high-quality diabetes care include regular review, patient registration and recall [19–21]. There has been a shift towards multidisciplinary shared management of complex patients across primary and secondary care settings, and structured management of stable diabetes in primary care with suitable organisational support [21, 22]. While quality improvement strategies targeting professionals and patients improve diabetes care and patient outcomes, strategies which target the entire system of chronic disease management, such as case management, team changes and patient registry, are associated with the largest benefits [23].

Diabetes services in Ireland

Over the last two decades in Ireland, a plethora of policies and reports have repeatedly called for evidence-based service developments seen in other countries [24]. A number of diabetes initiatives have emerged, led by healthcare professionals, to improve diabetes care at a local level but with inconsistent implementation of a comprehensive diabetes service nationally. The balance of care between primary and secondary care settings varies and includes traditional hospital-based management, shared care between GPs and hospitals, and structured primary care-led management. Care in general practice ranges from ad hoc opportunistic management to structured care characterised by patient registration, regular recall and review coordinated by practice nurses [25]. A national survey of GPs reported that less than half used a patient register and diabetes guidelines or engaged in routine recall of patients with diabetes. Less than 10 % had a formal shared protocol or ever had a joint meeting with the hospital diabetes team. There was deficient access to allied health services such as podiatry, dietetics and eye screening [26]. Within the hospitals, not all diabetes services are led by an endocrinologist. Endocrinology-led services in Ireland had more developed subspecialty clinics and greater access to specialist allied health professionals. However, waiting times for these services were longer and discharge rates to primary care were lower than for non-specialty led services [27]. The provision of structured diabetes care in general practice and shared care between settings has produced favourable results in Ireland in terms of processes and outcomes of care [28–31]. However, these models of care are not common-place and there is a dearth of information on the quality of routine diabetes management at a national level.

The National Diabetes Programme: a complex intervention to standardise care

Against this backdrop of variation in the type and quality of diabetes care, and a lack of dedicated strategic national planning and programme implementation, in 2010, a clinical programme for diabetes was established to standardise and improve care for people with diabetes in Ireland, known as the National Diabetes Programme (NDP) [32]. The NDP was one of a number of clinical care programmes set up under the auspices of the Directorate of Clinical Strategy and Programme in the Health Service Executive (HSE), the national health service in Ireland. The overarching goals of these programmes are to improve access to services, quality and safety of care, and cost effectiveness. These goals are achieved by bringing together representatives from various clinical disciplines to develop standardised patient pathways and evidence-based models of care [32]. Similar to the other programmes, the diabetes programme has a defined governance structure with a national clinical lead and programme manager, a clinical advisory group, and a national working group with the joint involvement of healthcare providers in primary, secondary and tertiary care [33]. There are also four regional Diabetes Services Implementation Groups (DSIGs), which are multidisciplinary regional networks established to inform the development and implementation of the National Diabetes Programme.

The specific aim of the NDP is to 'save the eyes, limbs and lives of people with diabetes' [33]. Like other large-scale service delivery innovations [34], a change in patient outcomes was to be achieved through the coordinated reorganisation of existing services, and the introduction of new services and supports for people with diabetes. Dedicated work streams were established for the implementation of a national retinopathy screening programme, a national model of care for the screening and treatment of diabetic foot disease, and a national model of integrated care for the management of diabetes across primary, secondary and tertiary care settings (Fig. 1).

Service innovations such as the NDP lead to both intended and unintended consequences. Evaluation provides an opportunity not only to identify and track these but also to identify multilevel barriers to implementation and conditions that make success and sustainability more likely. However, process evaluation is difficult to apply to complex services spanning organisational boundaries [35]. The NDP represents a number of complex interventions introduced into a complex social system, making it an appropriate subject for a realist evaluation. The realist evaluation approach, developed by Pawson and Tilley, goes beyond looking at whether a programme works or not, to try and understand which aspects of the programme work, for whom, in what circumstances [36, 37]. There is an inherent acknowledgement that a programme will work differently in different contexts; the aim is to understand what it is about a programme that leads to different outcomes [38].

According to Pawson and colleagues, complex service interventions are based on an underlying hypothesis of

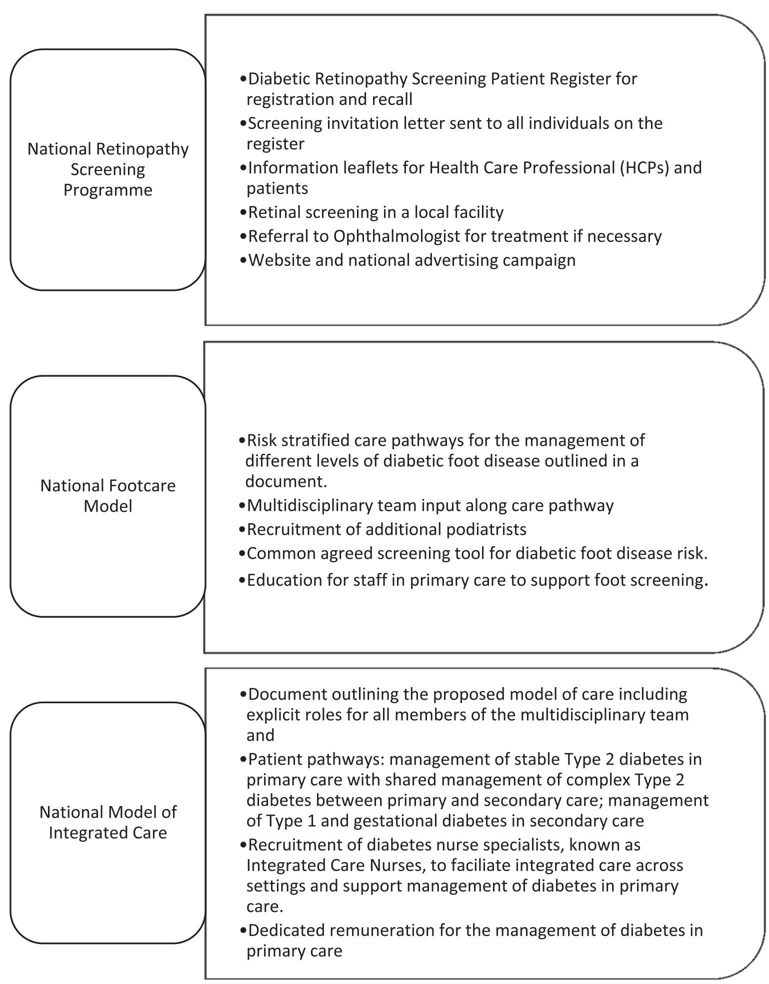


Fig. 1 Intervention components of the National Programme for Diabetes

how the intervention will bring about an outcome [37, 39]. The first step of a realist evaluation is to identify and articulate these theories, known as programme theories. A programme provides a resource, an opportunity or a constraint, that influences the decision-making process of its intended target group. It is this decision-making process that determines whether an outcome is achieved or not; complex interventions are active, that is they only work through stakeholders' reasoning and responses. This underlying interaction between what a programme provides and the reasoning of its intended targets is known as a mechanism. Understanding and explaining the often invisible implicit mechanisms are core functions of a realist evaluation [37, 40]. Mechanisms are argued to be triggered, to a greater or lesser extent in certain favourable and unfavourable contexts, leading to intended and unintended outcomes. The programme theory articulates a theoretical relationship between a context, mechanism and outcome, known as a 'C-M-O' configuration [37].

In this paper, we present the protocol for an evaluation of the NDP that adopts a realist approach. The aim of the evaluation is to identify and explain which aspects of the programme are working (or not working), for whom and in what circumstances to produce outcomes. The evaluation will examine three ongoing work streams of the NDP which have been prioritised since its inception in 2010: the introduction of a national diabetic retinopathy screening programme (initiated in 2013); the establishment of a national model of foot care for people with diabetes (staff recruited in 2013); and the development of a national model of integrated care for diabetes (staff recruited in 2013). The aim of this paper is to outline in detail the stages, methods and data being used in the evaluation, as well as some of the challenges to, and opportunities for, providing formative feedback to the NDP.

Methods/design

This prospective evaluation follows the research stages outlined by Pawson and Tilley: (1) elicit and formulate the programme theory underlying the NDP and its work streams (national retinopathy screening programme, national foot care model and national model of integrated care), (2) collect data to test these initial theories, (3) analyse data to interrogate the theories and (4) interpret analysis to refine or revise the initial programme theories [36] (Fig. 2).

Realist evaluation is method neutral and most studies employ both quantitative and qualitative research methods [41–44]. We are using mixed methods depending on the stage of the study and the theory component (context, mechanism or outcome) under scrutiny; for example documentary analysis and qualitative interviews are considered useful for identifying the official programme theory and context, qualitative interviews are also appropriate for exploring stakeholders' responses to and reasoning about the programme (mechanisms), and quantitative administrative data allow examination of outcomes such as service uptake [37]. Table 1 summarises the methods being used during data collection at stage 1 and stage 2.

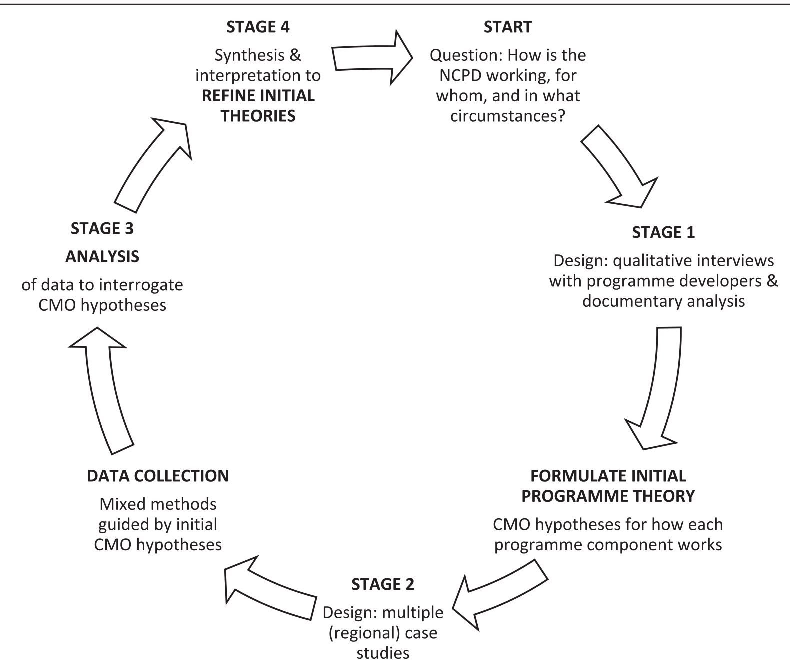


Fig. 2 Realist research cycle (adapted with permission from [63])

Table 1 Data collection during stages 1 and 2 to formulate and refine programme theories

Stage	Methods
Stage 1: Elicit and formulate the programme theory	• Documentary analysis of published and unpublished documents pertaining to the establishment, development and implementation of the National Programme for Diabetes and the three programme interventions. • Semi-structured interviews with national level programme developers ($n = 19$).
Stage 2: Data Collection	Implementation of the National Programme for Diabetes • Multiple case study design ($n = 4$ cases) • Semi-structured interviews with theoretically sampled stakeholders in each area ($n =$ approx. 15 per case).
	Further data for each case will be gathered through a number of sub-studies conducted at a local and national level to build a rich case description and allow for embedded analysis of each programme component.
	Retinopathy screening programme • Audit of registration, consent and uptake among a convenience sample of two large primary care centres ($n = 22$ GPs, approx. 600 people with diabetes) and a smaller rural practice in one region ($n = 2$ GPs, approx. 100 people with diabetes) • Semi-structured interviews with people with diabetes from those practices
	National foot care model • Semi-structured interviews with podiatrists including those recruited as part of the programme. • Cross-sectional study of administrative activity data submitted by podiatrists as part of the National Programme for Diabetes.
	National model of integrated care • National survey of Diabetes Nurse Specialists (DNSs) including those recruited as part of the programme. • Follow-up interviews and focus groups • Cross-sectional analysis of administrative activity data submitted by DNSs recruited as part of the National Programme for Diabetes

Stage 1: elicit and formulate the programme theory

Design

As a theory-based evaluation approach, the first step of the realist evaluation is to clarify the 'programme theory'; that is how the NDP and its three work streams are expected to cause or contribute to outcomes. The programme theory articulates the relationship between a context, mechanism and outcomes of the national programme components, known as 'C-M-O' configurations.

Data collection

Three data sources were used to develop the initial programme theory. Firstly, a documentary analysis was carried out to establish the official programme theory, expectations and rationale for establishing the Programme. Documents included published and unpublished material such as strategy documents from interest groups, media coverage, press releases, national service plans, NDP website, and official documentation on the role and function of the programmes. An additional file outlines the type and source of documents (see Additional file 1). These data were also useful for mapping the context in which the programme was being designed and implemented.

Secondly and concurrently, we conducted qualitative interviews with a purposive sample of stakeholders involved at a national level in the design, development and management of the Programme. All members of the national diabetes working group were invited to take part (membership between July 2014 and January 2015) as well as former clinical leads and programme managers. The national diabetes working group comprises representatives from endocrinology, general practice, diabetes nurse specialists and practice nurses, dietetics, podiatry, community pharmacy, public health, patient advocacy and health service management. Members also represent different parts of the country. Following an initial invitation via email, all participants were contacted individually by a member of the research team (MT) to outline the study and arrange a convenient time and place for interview.

A semi-structured topic guide was developed informed by initial findings from the documentary analysis and previously published realist evaluations [38, 42]. The topic guide was piloted with a convenience sample of two participants involved in diabetes care, who were not members of the national working group but were aware of the work of the Programme. Minor amendments were made to the prompts and probes used within the topic guide. The topic guide addressed participants' role in the Programme, why the programme was established, the planned changes and how they were being implemented, progress to date, anticipated barriers and facilitators, and expected outcomes (see Additional file 2).

Face-to-face interviews were conducted (by MT) with 19 participants between July 2014 and January, 2015 (average duration 1 h). Participants received an information sheet and signed a consent form prior to the interview. These participants are implementers within their own local diabetes service as well as being involved in the design of programme at a national level. Thus, in addition to discussing planned implementation and expected outcomes (official programme theory), participants discussed their own experience of implementation, perceived outcomes in their area, and barriers encountered. Data collection and analysis were iterative to allow the gathering of further data on emergent themes and the topic guide was modified to accommodate emergent lines of inquiry.

Thirdly, following a presentation of preliminary findings, a short survey was conducted among attendees at the annual conference held by the NDP (November, 2015). Attendees, including healthcare professionals, patient representatives, health service managers and policy makers involved in or affected by the national programme, were invited to complete open-ended questions about which aspects of the national programme were working well, which aspects were not working as well, and why. Respondents were asked to indicate their professional role and the area of the country in which they worked. Thirty attendees completed the questionnaire (approximately 25 % response rate). Gathering the opinions of those involved in implementation from around the country allowed for further refinement and corroboration of the initial programme theories based on national stakeholders' accounts.

Data analysis

Interviews were audio-recorded, transcribed verbatim and imported into NVivo 10 software [45]. The framework approach [46] was used to systematically identify contexts (C), mechanisms (M), and outcomes (O) in the interview transcripts and documents, and chart hypothetical relationships between them (C-M-O configurations) to formulate programme theories for each programme component.

The Framework approach is sufficiently open to allow for novel themes to emerge inductively during analysis [47]. First, transcripts were read and re-read (familiarisation), followed by open coding to identify contexts, mechanisms and outcomes. Emergent concepts which did not fit explicitly with the C-M-O framework were also coded. Two researchers (MT and SMH) open-coded three interviews of staff from different parts of the country. The research team then met to compare and contrast codes, clarify understanding of contexts, mechanisms and outcomes, and agree on an initial coding framework. Two independent coders (FR, KON, researchers who had recently joined the research team) were invited to analyse four interviews (from different professional backgrounds and locations) to further refine the coding framework. This coding framework was applied to subsequent transcripts by the research team. Framework development was a dynamic process with regular meetings to discuss new codes or merging existing codes, assumptions, and ideas about C-M-O configurations.

Having openly coded all of the transcripts, data were sorted and synthesised by theme bringing similar concepts together (thematic charting). At this stage, themes were sorted under the individual programme components: national working group (SMH), retinopathy screening (MT), national foot care model (KON) and national model of integrated care (FR). Each researcher led on the synthesis of codes and development of themes for a different programme intervention. This facilitated data management but also enabled data immersion necessary to develop a programme theory about the relationship between contexts, mechanisms and outcomes for that intervention. In some instances, participants themselves outlined partial C-M-O configurations during interviews (e.g. between contexts and outcomes, mechanisms and outcomes); these relationships were refined or revised by examining other participant interviews. However, in most cases, the research team developed C-M-O configurations based on the analysis of all interviews, starting with a synthesis of the proposed outcomes and working backwards to build a theory about the mechanism that led to that outcome and the context that triggered the mechanism.

Open-ended responses to the conference survey were coded using the same approach although emergent themes tended to reiterate, and overlap with enabling and disabling contexts identified during the interviews. The themes were used to reinforce or refine the initial C-M-O configurations.

Memos were used and shared throughout the analysis to note assumptions, events and changes in the NDP, coding definitions, hunches and early impressions [48]. The language and expressions of the participants were maintained as far as possible, using in vivo codes, to avoid losing the meaning and context. The results were presented to the wider research team for discussion.

Stage 2: data collection to test programme theories

The aim of stage 2, which is currently underway, is to collect data to test the C-M-O configurations developed in stage 1. A multiple case study design is being used. Case studies are often used in realist evaluation [34, 49–51]; this approach emphasises the in-depth study of phenomena in their real-life context, and the importance of theory to inform the design, selection and interpretation of case studies [52].

Case selection

A case was defined as a geographical area within one of the four HSE administrative regions (Fig. 3).

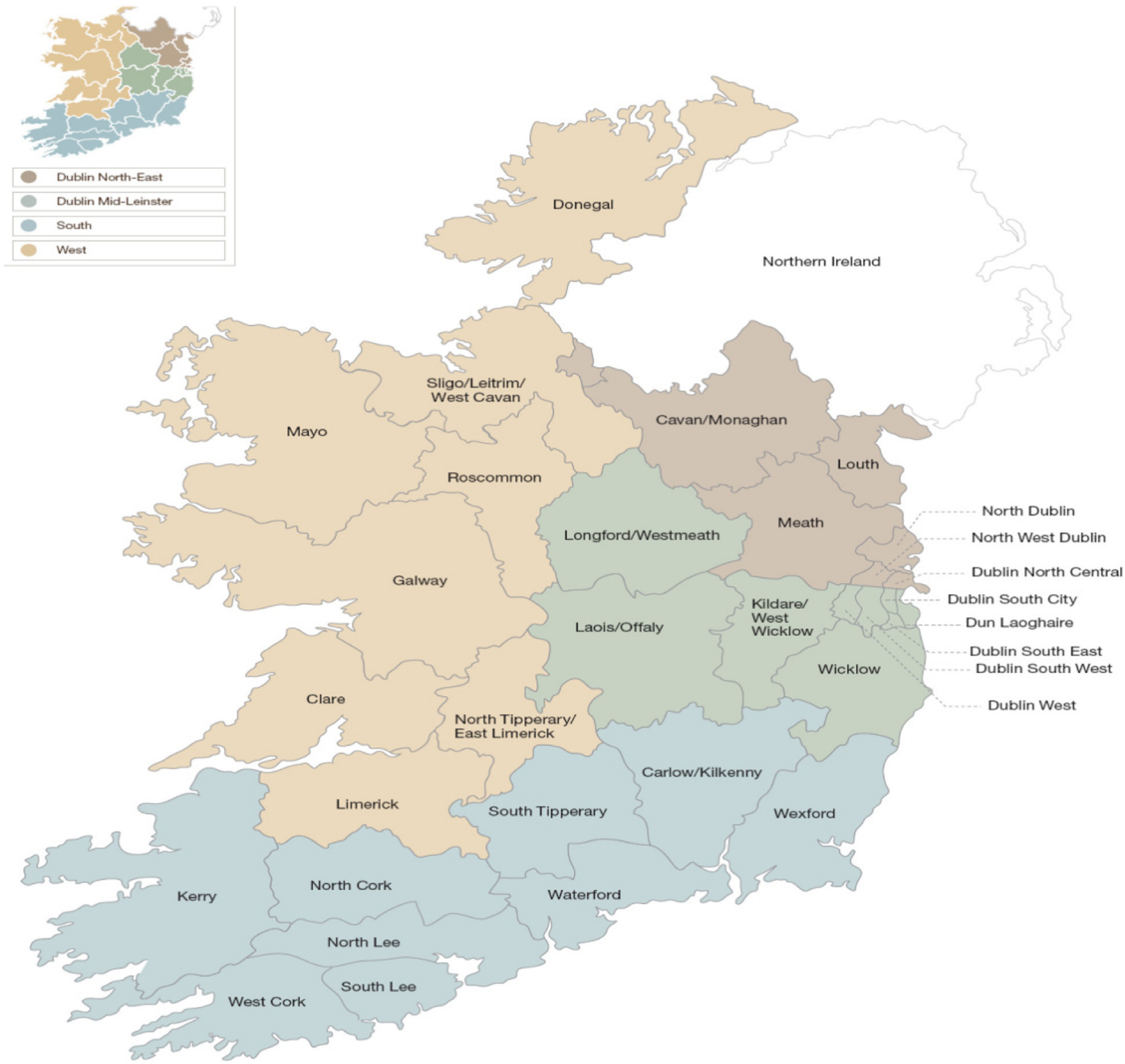


Fig. 3 Map of administrative regions in the Health Service Executive (HSE)

A number of criteria were used to select a case area. Firstly, cases had to have received an intervention from the NDP (retinopathy screening programme, integrated care nurse and/or podiatrist). Second, it emerged during stage 1 analysis that the presence or absence of a diabetes initiative (either a primary care-led diabetes initiative, an existing community diabetes nurse specialist (DNS) service, or an established diabetic retinopathy (DR) screening initiative) was an important contextual factor; therefore, we theoretically selected cases on this basis. More detail on the underlying rationale for case selection is available (see Additional file 3).

We mapped these criteria for all areas, starting with the allocation of interventions by the NDP, and discussed the selection of cases within the research team. Table 2 outlines the final selection of four cases and their characteristics.

Data collection

Within each case, multiple sources of data will be used to test the C-M-O configurations developed in stage 1.

Qualitative Qualitative interviews will be undertaken with key stakeholder groups purposively sampled in each case and this work is ongoing. Table 3 outlines the expected number of participants per case. In each area, local members of the regional DSIG will be invited to participate. Participants will be invited to suggest other

Table 2 Case study selection & sampling criteria

Case 1	Case 2	Case 3	Case 4
NDP interventions • Received 2 components Existing infrastructure and engagement • Prior DR screening initiative delivered in the community, open to patients in a select number of general practices (no universal access) • Existing primary care diabetes initiative with voluntary enrolment by some general practices	NDP interventions • Received 3 components Existing infrastructure and engagement • Previous population-based retinopathy screening initiative offered to all general practices in the area • Existing primary care diabetes initiative with voluntary participation from some practices • Community DNS	NDP interventions • Received 3 components Existing infrastructure and engagement • Previous hospital service which provided eye screening for those referred to service, no population-based screening programme in the community • Existing primary care diabetes initiative with voluntary participation from general practices • Community DNS	NDP interventions • Received 3 components Existing infrastructure and engagement • Previous hospital service which provided eye screening for those referred to service, no population-based screening programme in the community • No existing primary care-led diabetes initiative • Community DNS

Table 3 Stage 2 sample per case

	Number per case	Total
DSIG member	2	8
Endocrinologist	1	4
General practitioner (GP)	2	8
Practice nurse	2	8
Diabetes nurse specialist/integrated care nurse	2	8
Podiatrists	2	8
Ophthalmologist	1	4
Patient representative	2	8
Health service manager	1	4
Total	15	60

stakeholders such as health service managers that they engage with. These managers may or may not be formally involved with the DSIG but have a role in deploying and coordinating resources. Integrated care nurses and podiatrists appointed as part of the implementation of the NDP will be invited to participate in an interview or focus group, as well as diabetes nurse specialists (hospital and community-based) and podiatrists previously in post. A purposive sample of GPs and practice nurses will be recruited from practices enrolled/not enrolled in primary care-led diabetes initiatives. Participants will be recruited through educational meetings, continuing professional development groups and local DSIGs. People with diabetes will be recruited using a web-based entry form and dedicated telephone line (participant portal). To ensure we have patient representation specific to our cases, we will ask participating healthcare professionals to publicise our study and the participant portal to patients, and display sign-up posters in local clinics. People with diabetes will also be recruited through local education and awareness events run by a national patient advocacy group (Diabetes Ireland).

A theory-driven topic guide has been devised for interviews in stage 2, based on the programme theories developed during stage one. The topic guide has been tailored to the stakeholder group being interviewed (hospital specialist, GP, practice nurse, specialist nurse, podiatrist, person with diabetes). During the interview, we will have an active and explicit role in explaining the contexts and outcomes of interest, to ensure a shared understanding of the terminology and purpose of the questions. In the context of our developed theories, participants will be invited to explain how their experience fits with that theory and reflect on what may explain the outcomes in their area [53]. The topic guide has been piloted with a convenience sample of one GP and two practice nurses, staff who would be most familiar with or in receipt of most programme components. Written consent will be obtained prior to each interview, and all interviews will be audio-recorded and transcribed verbatim. Thematic analysis of the interviews will be guided by the initial programme theories identified in stage 1. However, analysis will be open to emergent themes to facilitate further theory refinement.

Quantitative To assess programme outcomes, administrative data and healthcare professional surveys will be analysed (see Table 1). For the national retinopathy screening programme, the outcomes being examined are registration, consent and uptake. These will be examined using local audits of clinical records in general practice. For the national foot care model, case-specific activity data including the number and risk profile of patients will be analysed. For the national model of integrated care, a national survey of diabetes nurse specialists (including integrated care nurses) is being conducted. This will be supplemented with case-specific analysis of activity data, including the number of GPs engaging with the integrated care nurse service and the number of patient consultations.

Stage 3: analyse data to interrogate theories

In realist evaluation, the unit of analysis is the theories hypothesising the mechanisms by which an intervention produces certain outcomes in a particular context [54]. A matrix will be used to analyse and synthesise both the qualitative and quantitative data available for each case (administrative data, survey data, transcripts) [55, 56]. A matrix will be constructed for each programme theory relating to various programme components (retinopathy screening, national foot care model, and national model of integrated care). Following the example of O'Cathain and colleagues [57], the columns of the matrix will contain the contexts, mechanisms and outcomes for a given theory. Each row in the matrix will represent a different case (see Additional file 4 for an example). This approach will facilitate within-case analysis, highlighting similarities or discrepancies between data sources which may lead to further data collection or analysis [56]. It will also facilitate cross-case analysis to identify patterns across cases. NVivo 10 software will be used to store and manage data [45].

Stage 4: interpret analysis to refine or revise the initial programme theories

In light of the analysis in stage 3, the programme theories underpinning the NDP will be refined. The original programme theories will be assessed against the evidence emerging within cases and then between cases to more accurately reflect the experiences of those delivering and receiving the changes introduced by the NDP, and the outcomes realised in different contexts.

Ethical considerations

This study has been approved by the Clinical Research Ethics Committee of the Cork Teaching Hospitals. Each participant in the study is asked for written informed consent prior to conducting the interviews and focus groups. Informed consent has also been sought from survey participants, and data have been anonymised for analysis and reporting. Permission has been granted by the NDP to analyse activity data submitted to the programme. Anonymity will be assured at each case study site and all participants will be given a unique ID number. Initial programme theories were presented to members of the national working group for comment. Results from later stages will be fed back to case study participants in the form of a case report. Any potentially identifiable information will be removed prior to reporting and publishing the findings.

Discussion

Realist evaluation, which allows for the study of context and its influence on outcomes, is appropriate for examining the implementation of the NDP, given the history of regional variation in diabetes services in Ireland. This paper outlines the protocol for a mixed methods evaluation to explore which aspects of the programme are working, for whom and in which circumstances.

Geographic case studies are often difficult to define [52], and this has been a particular challenge in this study given the ill-defined boundaries of health services in Ireland. Catchment areas for health services and hospitals are often fluid, and the organisational structures within the health service have gone through several recent reconfigurations. Furthermore, the results of stage 1 of this study suggest variation in diabetes services within regions and counties depending on the local resources, infrastructure and engagement from stakeholders such as GPs and local management. We have selected cases for stage 2 on the basis of these preliminary findings. The aim of this study is to understand how the NDP is working, for whom and in what circumstances. Therefore, the cases are considered instrumental as opposed to intrinsic [58], that is they are being used to gain a deeper understanding of programme implementation as a whole, as opposed to focusing on the uniqueness of the individual case itself.

We have used a number of strategies to enhance the rigour of this study. Data collection tools including topic guides and surveys have been extensively piloted. Different triangulation techniques will be used to strengthen the validity of findings, including the use of mixed methods, multiple data sources (interviews and documents) and researchers from different disciplinary perspectives (health services research, epidemiology, public health, clinical medicine) [59]. While the limitations of member checking as a strategy to verify overall results have been highlighted, it is considered appropriate to enhance validity in case study research, as case reports maintain the contextual information that allows participants to relate their experiences to synthesised results [52, 60].

Throughout this study, data will be collected and analysed concurrently within each stage to allow emergent lines of enquiry to be explored [60]. The research team has endeavoured to be responsive to the implementation of the programme and changeable context in which it is being rolled out. For example, in October 2015, the Department of Health in Ireland agreed a new contract with GPs which provided financial reimbursement for two structured diabetes review visits in general practice per year. This scheme is known as the Diabetes Cycle of Care. Patients with type 2 diabetes who have a medical card or a GP visit card, which entitles them to free GP care in Ireland, are eligible to be registered by their GP for the scheme. This is a significant influential factor in the context of the NDP. Although not part of the initial programme theories, given its recent introduction, we have adapted our topic guide to explore how the introduction of this financial incentive may influence implementation.

Complex social interventions such as the NDP achieve their outcomes by active input from various stakeholders. Qualitative research is an important part of exploring the reasoning and responses of stakeholders to a programme [37]. Similar to other realist evaluations [61], the results of our interviews with national programme stakeholders, who were also local implementers with context-specific experience, further refined ‘official’ programme theories about which aspects are working, in which circumstances and why. This evaluation builds on previous work by the research team which analysed the many diabetes care policies in Ireland, thereby providing information on some of the contextual factors that preceded the national programme [24]. Pawson suggests that by defining clearly the boundaries of case studies, evaluators are then able to harness the potential of administrative data, for example, relevant to quantifying the outcomes of programmes in realist evaluation [37]. Collaboration with the NDP has enabled us to analyse such administrative information where available. However, we are limited by the lack of a diabetes register in Ireland or national databases on the quality of diabetes care, and patients’ health service interactions and outcomes.

There is increasing interest in the evaluation of health policy and health service implementation. In particular, there is increasing emphasis on theory-based evaluations which aim to establish the context and mechanisms that facilitate successful implementation rather than simply focusing on the achievement of specific endpoints [35].

Realist evaluation has been used for this purpose to study a diverse range of service changes including the introduction of an integrated care pathway for palliative care [41], a multifaceted maternity care programme [49], 'communities of practice' [38], oncology teams [54] and quality improvement in primary care [51]. There are very few evaluations of the implementation of programmes or service interventions in Ireland, and to our knowledge, this is the first realist evaluation of a programme in Ireland.

The NDP is constantly moving between planning for future work streams and ongoing implementation of the current work streams. Therefore, the programme offers a potentially unique opportunity to evaluate and inform the implementation of changes in the Irish health system as they emerge and evolve. For example, there has been phased recruitment of integrated care diabetes nurse specialists (known as integrated care nurses (ICNs)) to support the implementation of the national model of integrated care as resources have been secured at national level. A protocol has been developed to clarify the role of the ICN, partly in response to barriers to implementation highlighted in the evaluation. There is close collaboration between the national working group and research team; the principal investigator (PK) is a member of the working group which provides an opportunity to provide formative feedback on implementation to those responsible. Our results should also provide insights relevant to the implementation of other clinical care programmes in Ireland operating in similar contexts. Furthermore, we hope that the findings will be relevant to programmes in other countries, some of which are also evaluating implementation of new care programmes [62].

Additional files

Additional file 1: Secondary sources of information included in documentary analysis. Description of data: details of documents used in documentary analysis during stage 1 (DOCX 24 kb)

Additional file 2: Topic guide stage 1. Description of data: topic guide used during semi-structured interviews in stage 1. (DOCX 22 kb)

Additional file 3: Case selection. Description of data: rationale for case selection. (DOCX 12 kb)

Additional file 4: Sample matrix. Description of data: an example of the matrix approach that will be used to integrate qualitative and quantitative data. (DOCX 11 kb)

Acknowledgements
The authors are grateful to the past and present members of the ESPIRIT research team who contributed to data management and discussions regarding the analysis and interpretation of the data: Caragh Flannery, Julie Barrett and Cora Grant. The authors are also grateful to all of the participants who have participated in the evaluation and those who facilitated access to data.

Funding
This work was funded by the Health Research Board Research Leader Award (RL/2013/7) awarded to PMK. PMK, MT, KON and FR are funded through this award. SMH is funded by the Centre for Ageing Research and Development in Ireland (CARDI). The funding body had no role in the study design, collection, analysis or interpretation of data.

Authors' contributions
SMH designed the study, conducted data analysis and wrote the initial draft of the paper. MT contributed to the study design, carried out data collection, conducted data analysis and contributed to revising the manuscript. FR contributed to the study design, carried out data collection, conducted data analysis and contributed to revising the manuscript. KON contributed to the study design, carried out data collection, conducted data analysis and contributed to revising the manuscript. NM contributed to the study design and revised the manuscript. PMK contributed to the study design and contributed to revising the manuscript. All authors have given final approval of the version to be published and agree to be accountable for all aspects of the work.

Competing interests
The authors declare that they have no competing interests.

Consent for publication
Not applicable.

Ethics approval and consent to participate
This study has been approved by the Clinical Research Ethics Committee of the Cork Teaching Hospitals. Each participant in the study is asked for written informed consent prior to conducting the interviews and focus groups. Informed consent has also been sought from survey participants, and data have been anonymised for analysis and reporting. Permission has been granted by the NDP to analyse activity data submitted to the programme.

Author details
[1]Department of Epidemiology & Public Health, Western Gateway Complex, University College Cork, Western Rd, Cork, Ireland. [2]Department of Health Services Research & Policy, London School of Hygiene and Tropical Medicine, 15-17 Tavistock Place, London WC1H 9SH, UK.

Received: 16 June 2016 Accepted: 30 June 2016
Published online: 28 July 2016

References

1. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care. 2004;27(5):1047–53.
2. Vos T, Barber RM, Bell B, Bertozzi-Villa A, Biryukov S, Bolliger I, Charlson F, Davis A, Degenhardt L, Dicker D, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study. Lancet. 2013;386(9995):743–800.
3. Franco OH, Steyerberg EW, Hu FB, Mackenbach J, Nusselder W. Associations of diabetes mellitus with total life expectancy and life expectancy with and without cardiovascular disease. Arch Intern Med. 2007;167(11):1145–51.
4. Wexler D, Grant R, Wittenberg E, Bosch J, Cagliero E, Delahanty L, Blais M, Meigs J. Correlates of health-related quality of life in type 2 diabetes. Diabetologia. 2006;49(7):1489–97.
5. Zhang P, Zhang X, Brown J, Vistisen D, Sicree R, Shaw J, Nichols G. Global healthcare expenditure on diabetes for 2010 and 2030. Diabetes Res Clin Pract. 2010;87(3):293–301.
6. Diabetes Care and Research in Europe. The Saint Vincent Declaration. Diabet Med. 1990;7(4):360–360.
7. Rothe U, Müller G, Schwarz PEH, Seifert M, Kunath H, Koch R, Bergmann S, Julius U, Bornstein SR, Hanefeld M, et al. Evaluation of a diabetes management system based on practice guidelines, integrated care, and continuous quality management in a federal state of Germany: a population-based approach to health care research. Diabetes Care. 2008;31(5):863–8.
8. Adolfsson ET, Rosenblad A, Wikblad K. The Swedish National Survey of the Quality and Organization of Diabetes Care in Primary Healthcare—Swed-QOP. Primary Care Diabetes. 2010;4(2):91–7.
9. Looker HC, Nyangoma SO, Cromie DT, Olson JA, Leese GP, Black MW, Doig J, Lee N, Lindsay RS, McKnight JA, et al. Rates of referable eye disease in the

Scottish National Diabetic Retinopathy Screening Programme. Br J Ophthalmol. 2014;98(6):790–5.
10. Gudbjörnsdottir S, Cederholm J, Nilsson PM, Eliasson B. The National Diabetes Register in Sweden: an implementation of the St. Vincent Declaration for Quality Improvement in Diabetes Care. Diabetes Care. 2003;26(4):1270–6.
11. DCCT: The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med. 1993;329(14):977–86.
12. UKPDS: UK Prospective Diabetes Study Group. Intensive blood-glucose control with sulphonyureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes. Lancet. 1998;352(9131):837–53.
13. Holman R, Paul S, Bethel M, Matthews D, Neil H. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med. 2008;359(15):1577–89.
14. Holman RR, Paul SK, Bethel MA, Neil HAW, Matthews DR. Long-term follow-up after tight control of blood pressure in type 2 diabetes. N Engl J Med. 2008;359(15):1565–76.
15. Cholesterol Treatment Trialists Collaborators. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90056 participants in 14 randomised trials of statins. Lancet. 2008;366(9493):1267–78.
16. NICE. Type 2 diabetes in adults: management. London: National Institute for Health and Care Excellence; 2015.
17. Harkins V. A practical guide to integrated type 2 diabetes care. Dublin: Irish College of General Practitioners; 2016.
18. American Diabetes Association. 4. Foundations of care: education, nutrition, physical activity, smoking cessation, psychosocial care, and immunization. Diabetes Care. 2015;38(Supplement 1):S20–30.
19. Renders CM, Valk GD, Griffin S, Wagner E, Eijk J, Assendelft W: Interventions to improve the management of diabetes mellitus in primary care, outpatient and community settings.Cochrane Database Syst Rev. 2000;Issue 4:Art. No.: CD001481
20. Wagner EH, Austin BT, Von Michael K. Organizing care for patients with chronic illness. Milbank Q. 1996;74(4):511–44.
21. Griffin S, Kinmonth AL. Diabetes care: the effectiveness of systems for routine surveillance for people with diabetes. Cochrane Database Syst Rev. 2000;2:CD000541.
22. Kahn R, Anderson JE. Improving diabetes care: the model for health care reform. Diabetes Care. 2009;32(6):1115–8.
23. Tricco AC, Ivers NM, Grimshaw JM, Moher D, Turner L, Galipeau J, Halperin I, Vachon B, Ramsay T, Manns B, et al. Effectiveness of quality improvement strategies on the management of diabetes: a systematic review and meta-analysis. Lancet. 2012;379(9833):2252–61.
24. Mc Hugh SM, Perry IJ, Bradley C, Brugha R. Developing recommendations to improve the quality of diabetes care in Ireland: a policy analysis. Health Res Policy Syst. 2014;12(1):53.
25. Mc Hugh S, O'Mullane M, Perry IJ, Bradley C. Barriers to, and facilitators in, introducing integrated diabetes care in Ireland: a qualitative study of views in general practice. BMJ Open. 2013;3(8):e003217.
26. Mc Hugh S, O'Keeffe J, Fitzpatrick A, de Siún A, O'Mullane M, Perry I, Bradley C. Diabetes care in Ireland: a survey of general practitioners. Prim Care Diabetes. 2009;3(4):225–31.
27. O'Donnell M, de Siún A, O'Mullane M, Smith D, Bradley C, Finucane F, Dinneen S. Differences in the structure of outpatient diabetes care between endocrinologist-led and general physician-led services. BMC Health Serv Res. 2013;13(1):493–8.
28. Mc Hugh SM, Marsden P, Brennan C, Murphy K, Croarkin C, Moran J, Harkins V, Perry I. Counting on commitment; the quality of primary care-led diabetes management in a system with minimal incentives. BMC Health Serv Res. 2011;11(1):384–93.
29. Brennan C, Harkins V, Perry I. Management of diabetes in primary care: a structured-care approach. Eur J Gen Pract. 2008;14(3):117–22.
30. Smith S, Bury G, O'Leary M, Shannon W, Tynan A, Staines A, Thompson C. The North Dublin randomized controlled trial of structured diabetes shared care. Fam Pract. 2004;21(1):39–45.
31. Collins MM, O'Sullivan T, Harkins V, Perry IJ. Quality of life and quality of care in patients with diabetes experiencing different models of care. Diabetes Care. 2009;32(4):603–5.
32. Royal College of Physicians Ireland. About the National Clinical Programmes [https://www.rcpi.ie/national-clinical-programmes/]. 01.03.16
33. Health Service Executive. National Clinical Programme for Diabetes [http://www.hse.ie/eng/about/Who/clinical/natclinprog/diabetesprogramme/]. 01.03.16
34. Greenhalgh T, Humphrey C, Hughes J, Macfarlane F, Butler C, Pawson R. How do you modernize a health service? A realist evaluation of whole-scale transformation in London. Milbank Q. 2009;87.
35. Lamont T, Barber N, Pury JD, Fulop N, Garfield-Birkbeck S, Lilford R, Mear L, Raine R, Fitzpatrick R. New approaches to evaluating complex health and care systems. BMJ. 2016;352. i154.
36. Pawson R, Tilley N. Realistic evaluation. London: Sage; 1997.
37. Pawson R. The science of evaluation: a realist manifesto. London: Sage; 2013.
38. Ranmuthugala G, Cunningham FC, Plumb JJ, Long J, Georgiou A, Westbrook JI, Braithwaite J. A realist evaluation of the role of communities of practice in changing healthcare practice. Implement Sci. 2011;6:49.
39. Pawson R, Greenhalgh T, Harvey G, Walshe K. Realist review—a new method of systematic review designed for complex policy interventions. J Health Serv Res Policy. 2005;10 suppl 1:21–34.
40. Dalkin SM, Greenhalgh J, Jones D, Cunningham B, Lhussier M. What's in a mechanism? Development of a key concept in realist evaluation. Implement Sci. 2015;10(1):1–7.
41. Dalkin SM, Jones D, Lhussier M, Cunningham B. Understanding integrated care pathways in palliative care using realist evaluation: a mixed methods study protocol. BMJ Open. 2012;2:e001533. doi:10.1136/bmjopen-2012-001533.
42. Abhyankar P, Cheyne H, Maxwell M, Harris FM, McCourt C. A realist evaluation of a normal birth programme. Evid Based Midwifery. 2013;11(4):112–9.
43. Rycroft-Malone J, Fontenla M, Bick D, Seers K. A realistic evaluation: the case of protocol-based care. Implement Sci. 2010;5(1):38–52.
44. Goicolea I, Hurtig AK, San Sebastian M, Vives-Cases C, Marchal B. Developing a programme theory to explain how primary health care teams learn to respond to intimate partner violence: a realist case-study. BMC Health Serv Res. 2015;15:228.
45. QSR International Pty Ltd. NVivo qualitative data analysis software, Version 10. 2012.
46. Ritchie J, Lewis J. Qualitative research practice: a guide for social science students & researchers. Thousand Oaks: Sage Publications; 2003.
47. Mays N, Pope C. Qualitative research in health care, 3rd edn. Malden, MA: Blackwell Publishing; 2006
48. Charmaz K. Constructing Grounded Theory: a practical guide through qualitative analysis. London: Sage Publications Ltd; 2006.
49. Cheyne H, Abhyankar P, McCourt C. Empowering change: realist evaluation of a Scottish Government programme to support normal birth. Midwifery. 2013;29(10):1110–21.
50. Tremblay D, Touati N, Roberge D, Denis J-L, Turcotte A, Samson B. Conditions for production of interdisciplinary teamwork outcomes in oncology teams: protocol for a realist evaluation. Implement Sci. 2014;9(1):1–11.
51. Schierhout G, Hains J, Si D, Kennedy C, Cox R, Kwedza R, O'Donoghue L, Fittock M, Brands J, Lonergan K, et al. Evaluating the effectiveness of a multifaceted, multilevel continuous quality improvement program in primary health care: developing a realist theory of change. Implement Sci. 2013;8(1):1–15.
52. Yin RK. Case study research: design and methods. 4th ed. Thousand Oaks, CA: Sage; 2009.
53. Pawson R. Theorizing the interview. Br J Sociol. 1996;47(2):295–314.
54. Randell R, Greenhalgh J, Hindmarsh J, Dowding D, Jayne D, Pearman A, Gardner P, Croft J, Kotze A. Integration of robotic surgery into routine practice and impacts on communication, collaboration, and decision making: a realist process evaluation protocol. Implement Sci. 2014;9(1):52.
55. Miles MB, Huberman AM. Qualitative data analysis: an expanded sourcebook: Sage; 1994
56. O'Cathain A, Murphy E, Nicholl J. Three techniques for integrating data in mixed methods studies. BMJ. 2010;341:c4587.
57. O'Cathain A, Murphy E, Nicholl J. Multidisciplinary, interdisciplinary, or dysfunctional? Team working in mixed-methods research. Qual Health Res. 2008;18(11):1574–85.
58. Stake R. Case Studies. In: Denzin N, Lincoln Y, editors. Strategies of qualitative inquiry. Thousand Oaks: Sage Publications; 1998.
59. Farmer T, Robinson K, Elliott SJ, Eyles J. Developing and implementing a triangulation protocol for qualitative health research. Qual Health Res. 2006;16(3):377–94.

60. Morse JM, Barrett M, Mayan M, Olson K, Spiers J. Verification strategies for establishing reliability and validity in qualitative research. Int J Qual Methods. 2008;1(2):13–22.
61. Bartlett YK, Haywood A, Bentley CL, Parker J, Hawley MS, Mountain GA, Mawson S. The SMART personalised self-management system for congestive heart failure: results of a realist evaluation. BMC Medical Informatics and Decision Making. 2014;14(1):1–13.
62. Raaijmakers LGM, Kremers SPJ, Schaper NC, de Weerdt I, Martens MK, Hesselink AE, de Vries NK. The implementation of national action program diabetes in the Netherlands: lessons learned. BMC Health Serv Res. 2015;15(1):1–8.
63. Marchal B, Belle S, Olmen J, Hoerée T, Kegels G. Is realist evaluation keeping its promise? A literature review of methodological practice in health systems research. Evaluation 2012;18.